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Editorials

- 19 THEY ALSO SERVE
- 19 THE TRIUMPH
- 20 MEDICAL LOSS LEADERS

Articles

- 21 COLORADO TICK FEVER
Carl M. Eklund, Richard C. Kennedy and Mary Casey, Hamilton, Montana
- 25 OCULAR ARCERIA
Roger C. Seyferth, D.D.S., M.D., Elko, Nevada
- 26 SIMPLE GUIDES IN THE NON-EMERGENCY TREATMENT OF DIABETES MELLITUS
Jacobus H. Verhave, M.D., Portales, New Mexico
- 31 PYELONEPHRITIS
John L. Emmett, M.D., Rochester, Minnesota
- 40 CARDIAC SOUNDS AND MURMURS IN CHILDREN
Colin H. M. Walker, M.D., Denver

Organization

- 60 COLORADO
- 60 MONTANA
- 60 NEW MEXICO
- 61 UTAH—HOUSE OF DELEGATES PROCEEDINGS
- 66 WYOMING

Features

- 52 WASHINGTON SCENE
- 66 MEDICAL SCHOOL NOTES
- 68 NATIONAL AFFAIRS
- 68 BLUE CROSS-BLUE SHIELD
- 71 TUMOR CONFERENCE—MALIGNANT MESOTHELIOMA

78-79 WANT ADS
81 INDEX TO ADVERTISERS

Meetings—Programs

- 39 ANNOUNCEMENT OF COLORADO STATE MEDICAL SOCIETY ANNUAL SESSION
- 58-59 15TH ANNUAL ROCKY MOUNTAIN CANCER CONFERENCE

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AS A HIGH SCHOOL STUDENT, I can recall with mental anguish the task of having to "commit to memory" many bits of literary poetry and prose.

Probably the greatest mass of apparently senseless jargon that was crammed into my cranium was Milton's Sonnet on His Blindness. I firmly believe that the logarithm table

would have been easier to memorize. Frankly, several years were required for me to fully comprehend the true meaning of these words so beautifully penned by Milton. Here was a blind man, obviously for a while despondent and critical, but when the blue chips were down, he was fully prepared to volunteer for service when the need came.

Two and a half centuries have passed since this sonnet was written, but the philosophy expressed is more urgent today than then. Today it is becoming increasingly more important to be "prepared." Not everyone can be Chief of Staff of his hospital, or President of his county or state medical society or the American Medical Association. But there is one thing for certain; every physician can *prepare* himself for that job which may be his today or tomorrow. This holds true in his professional field in being alert to recognize some rare or bizarre medical or surgical problem and then being able to cope with it. Then, too, it involves the moral responsibility and obligation each American physician owes to his colleagues and to his life's work in being informed as to just what he may be called upon to do to help preserve one of our American freedoms—freedom of choice!

The clamor in this Congress for an increase in and the broadening of the coverage of the Welfare State has already been exhibited. It is our duty and our obligation to inform ourselves of the job that lies before us. Each of us should be as enlightened as the President of his medical society or the chairman of his Legislative Committee.

It may be that at the drop of a hat we will have the opportunity to give a few extemporaneous remarks at a service club meeting, a P.T.A. gathering or even at the "bull session" in the locker room of the country club.

Every opportunity to enlighten our patients and the public must be capitalized. Ours is the job of selling a product—and that product is the continuation of a patient-physician relationship that has been the right and privilege of Americans for generations.

An informed man is a forceful and strong man.

"They also serve who only stand and wait."

Family Doctor

THE HUE AND CRY WAS OVER. The well planned attack of organized labor combined with the desire of the politicians to get the "elder citizen" vote had succeeded in socializing another segment of society. A masterstroke

The Triumph

had been achieved and the bill had been signed into law by the President. The BARBERS had been socialized. They had argued without avail that the legislation would deprive them of their constitutional rights, that it would result in overusage, that the government could not afford it and that the problem could best be solved by the tried and true system of free private enterprise. But the fight was over. The vanquished returned to work hoping that the effects would not be as bad as they feared. There was one consolation. Wishing to get support from the barbers the statesmen had guaranteed that the price of haircuts would increase from \$1.75 to \$2.50. That was their consolation prize. Now it was "free" haircuts for all.

The citizens of each community were assigned to a barber and each barber had his list or panel of customers. He was responsible

for their tonsorial needs. He was surprised the first morning when he opened the door to find 20 people waiting to get into his shop. Usually no one arrived for at least 30 to 60 minutes. He was further shocked to find folks whose hair had been cut only a few days before. By the time he had finished cutting the hair of the first two townspeople ten more had entered his shop. It was soon obvious that if he were to keep up he would have to cut hair faster. The clipper became the only instrument. Shaping with scissors stopped. The neck shave, the sideburns, and the butch cut were too time consuming to continue. Rapidly the time was trimmed down to three minutes per customer. It was a fast, thrilling race. In the chair (no time for neck-tape), sheet over clothing, clipper racing, sheet off—NEXT. This grueling pace continued day after day. In order to keep up he had to open the shop earlier and close it later. Those who used to have their hair cut every two weeks now came in every four to five days. Anyone with a few minutes off or who wanted to loaf awhile dropped in and had his hair cut.

Anyway it was lucrative—and then the blow fell. The response of the public to this free service was a complete surprise to the governmental officials. Although the same thing had occurred in England a few years earlier, they had refused to believe that it could happen here. The funds simply were not sufficient. Something had to be done. The first solution considered was a limit on the number of haircuts per year. The repercussion at the polls would be terrific however, and this scheme died immediately. There was only one answer. The price of haircuts must go down! The barbers let out a roar, but it was drowned out by the editors and the T.V. current events analysts who pointed out that they were overpaid anyway and had been gouging the public for years and furthermore deserved just what they got. The barber kept trying but his heart wasn't in his work. The quality of even the three-minute haircut worsened. Complaint after complaint was filed by the taxpayers with the barber's political superior. They wanted to change barbers but the panels were all filled. It was him or no one.

The hue and cry is over. The endless lines

of people troop in and out of the barber shop but there are no smiles on their faces and their heads show the effect of speed. Their barber isn't smiling either. He is dizzy from the pace, his pride is gone and he looks forward with weary thoughts to the governmental records he must fill out when he finally gets home.

Hugh S. Collett, M.D.
(Elko, Nevada)

DURING THE SUMMER SLUMP (is there such a thing?) try a few of the merchandising gimmicks of your fellow business men. [Don't you dare!—Ed.] They're guaranteed to work, even the "loss leaders," and they've always

been acceptable as routine promotions by the public. Here are a few samples.

Medical

Loss Leaders

Tack them on the bulletin board, hang them out the

window—or include them, one or two at a time, in the monthly billings (be sure and send them to the paid up customers as well!!).

"This week only—two camp physicals for the price of one."

"Second camp physical only \$1.00 with purchase of first exam."

"Hemoglobin determination free with every blood sugar test this month."

"Get them while they last—limited item—outdated flu vaccine only \$1.50 per shot."

"Green stamps with every paid up office visit. Bonus: Double stamps during September."

"Get your blood test now before price advances scheduled for October."

"One polio shot free for every new customer giving your name."

With a little reflection and imagination you too can think up advertising slogans and gimmicks for the medical profession. Mail us your best ideas and we'll publish them in the next issue. A six month subscription to Cervi's Journal for the best slogan. No box-tops, please.

J.H.



Remember the dates—July 12-13—and attend the Rocky Mountain Cancer Conference in Denver. See program, pages 58 and 59.

Colorado tick fever*

Carl M. Eklund, Richard C. Kennedy, and Mary Casey, Hamilton, Montana

Some sidelights on a disease usually considered benign. Bleeding and CNS involvement may occur, especially in children.

SOON AFTER THE FIRST DESCRIPTION of Rocky Mountain spotted fever, it was recognized that a relatively benign febrile disease without rash sometimes followed tick bite¹ but it was not until the publications of Becker in 1926 and 1930^{2,3} that evidence was presented to indicate that the milder disease syndrome was not a form of spotted fever. Becker found that guinea pigs inoculated with the blood of such patients did not become sick and that rickettsiae could not be demonstrated in their tissues.

Clinical course

The first detailed clinical account of this disease was given by Topping and associates⁴ in 1940, when they studied 11 patients in Colorado. They found that patients became suddenly ill four to five days after tick bite with chills, or chilly sensations, severe general aching, and fever up to 103°. These symptoms continued for two or three days; there was then usually a remission of two days, generally followed by a recurrence of symptoms which lasted another one or two days. A leucopenia was found in eight cases in which a white blood count was done. Also a questionnaire was sent to Colorado physicians and data were thus obtained on 53 addi-

tional patients. Fever, headache, chills, and backache were the most frequently reported symptoms. In these reported cases there were 39 with two febrile periods; first period ranged from two to seven days, remission one to seven days, and second febrile period one to 11 days. Florio, et al., in 1944⁵ reproduced the above-described clinical syndrome in volunteers by inoculation of serum from patients with the naturally acquired disease. Persons immunized against Rocky Mountain spotted fever were also susceptible to infection by such serum which provided further evidence that this disease syndrome was not a mild form of spotted fever. Inoculation of hamsters with blood of patients caused a lowering of the white blood count. This leucopenia could be reproduced in a series of hamsters by serial transmission of blood. In 1946 Florio, et al.,⁶ reported that the agent which had been passed serially in hamsters caused infection in a volunteer after passage through a Seitz EK filter and through a gradacol membrane of 181 m μ average pore diameter and concluded that the causative agent of Colorado tick fever (CTF) was a virus. Three of Florio's hamster strains of virus were adapted to adult mice by Koprowski and Cox^{7,8} and they isolated one strain of virus directly from a patient's blood by use of mice.

A relatively simple method for establishing a diagnosis was made available when Oliphant and Tibbs⁹ readily isolated virus from the blood of patients by the intraperitoneal inoculation of 3-4-day-old mice. By the use of this technic at the Rocky Mountain Laboratory, virus has been isolated from the blood of 552 patients. Blood samples were examined from all patients where there was

*U. S. Department of Health, Education, and Welfare, Public Health Service, National Institutes of Health, National Institute of Allergy and Infectious Diseases, Rocky Mountain Laboratory, Hamilton, Montana.

possibility of tick exposure regardless of the physicians' clinical impressions as to the etiology of the disease. Data submitted by attending physicians concerning these patients have given valuable information regarding the geographic and seasonal distribution of this disease, the period during which virus is present in the blood, the time of appearance of antibodies, and the occurrence of unusual forms of the disease. In a previous summary of some of these data¹⁰, reference was made to the fact that some patients from whom virus was isolated were reported to have central nervous system symptoms or severe bleeding. Fitz and Meiklejohn¹¹ have presented cases with central nervous system symptoms. The present paper gives a brief summary of all the data collected by the Rocky Mountain Laboratory in hope that it may stimulate physicians to gather more information regarding the clinical picture to be expected in CTF.

Laboratory diagnosis

In any infectious disease, diagnosis is best made by isolation of the infectious agent. Isolation is difficult in most virus diseases because the viruses usually survive for only short periods at room temperature and it is therefore necessary to send refrigerated specimens to a laboratory. However, CTF virus is stable for several days in whole blood at room temperature so shipment of blood specimens can be made without refrigeration. Furthermore, since the virus apparently is present in the blood throughout the febrile period, the time of taking blood specimens is not critical. Figure 1 summarizes data as to day on which viremia was found. There has been no opportunity to examine daily blood specimens from a single patient, but data obtained from many different patients probably give a fair representation of the period during which virus is present in the blood. The long periods of viremia indicated in the figure may represent errors as to date of onset.

At this laboratory it is always the practice to attempt reisolation of the virus from the blood clot to protect against any laboratory error; and if the clinical picture is unusual, a further attempt is made to establish the virus isolated as the cause of the disease by

showing that, while there were no antibodies present against this virus in the acute blood specimen, they appeared during convalescence.

Diagnosis may also be established without virus isolation by showing an antibody rise in paired blood specimens taken during the acute illness and convalescence, but this is a slow method since at least three weeks elapse before neutralizing antibodies appear and four weeks before complement-fixing antibodies are present. The most satisfactory and rapid method of diagnosis is by isolation of virus as this requires only a week after receipt of the blood specimen.

Geographic distribution

Figure 2 and Table 1 show the areas where the patients acquired the disease. The data must not be interpreted as giving an accurate picture of the frequency of occurrence of

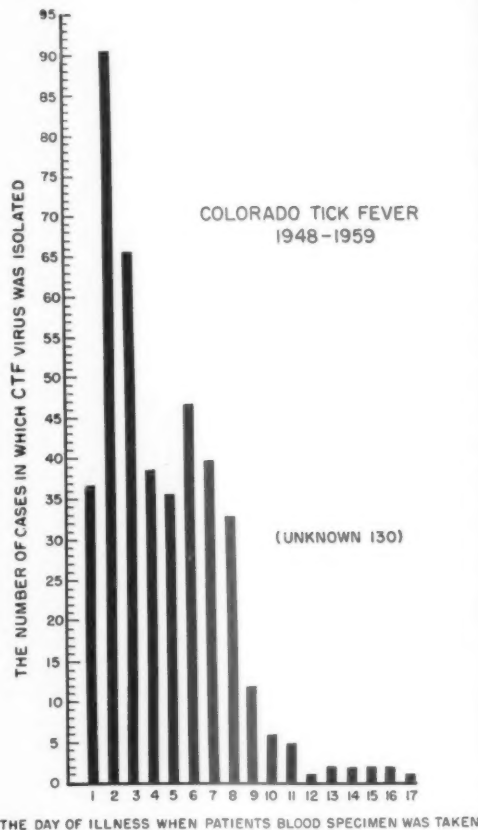


Fig. 1

the disease in the various areas since a relatively small number of physicians send in blood specimens, but the region in which the disease can be expected is probably repre-

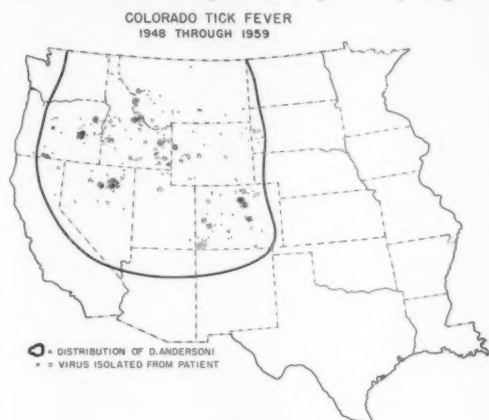


Fig. 2

sented accurately since virus has not been isolated from blood specimens examined each tick season from patients living in adjoining areas and with histories of tick exposure. Also virus has been isolated from ticks only within the distribution of *Dermacentor andersoni* or just west of this distribution. Cases have been reported from all states in the Rocky Mountain area and there is a pocket of infection in the Black Hills of South Dakota. More cases are reported from mountain areas and they extend over a longer period of the year.

Seasonal incidence

The seasonal occurrence is given in Table 2. Dates of onset have been from March 1 to October 14. The seasonal incidence varies from year to year; in an early spring, cases appear in March; in a late spring, cases may

TABLE 1
Colorado tick fever* geographic distribution, 1948-1959

Isolation by States	1948	1949	1950	1951	1952	1953	1954	1955	1956	1957	1958	1959	Totals
California.....							2			2			4
Colorado.....	1	2	3	2	7	7	15	17	13	30	26	5	128
Idaho.....					12	14	25	19	17	28	23	4	142
Oregon.....	3			1	4	5	13	6	10	11	20	6	79
Montana.....				1	5	3	9	7	5	6	7	2	45
Nevada.....					10	10	8	8	10	24	6	4	80
South Dakota.....								3	2	5	1	1	12
Washington.....					1								1
Wyoming.....	2	1	2	1	2	4	6	5	1	11	9	5	49
Utah.....		1		1	1	1	2	3	1	1	1		12
TOTALS.....	6	4	5	6	42	44	80	68	59	118	93	27	552

*Virus isolated at Rocky Mountain Laboratory from blood of patients.

TABLE 2
Colorado tick fever seasonal occurrence, 1948-1959

State	March	April	May	June	July	August	September	October	Unknown
California.....		1			2				1
Colorado.....	1	16	32	45	15	7	1		11
Idaho.....	1	11	38	49	32	5	1		5
Montana.....		5	11	10	15	2			2
Nevada.....	2	11	22	34	6	1			4
Oregon.....	2	14	21	24	10	2		1	5
South Dakota.....			6	4	2				
Utah.....			2	6	2				2
Washington.....			1						
Wyoming.....			17	16	12	1			3
TOTALS.....	6	58	150	188	96	18	2	1	33

not occur until late in April. Since the majority of patients give a history of tick bite or tick exposure, the seasonal distribution of cases is a reflection of tick activity.

Age and sex incidence

All ages except very young children have been affected but reported cases have been chiefly adult males engaged in activities that bring them in contact with ticks (Table 3). It is interesting to note that 22 cases have appeared in girls aged 5 to 9.

TABLE 3
Colorado tick fever age and sex
distribution, 1948-1959

Ages	Male	Female
0-4	5	5
5-9	23	22
10-14	15	9
15-19	23	2
20-24	37	3
25-29	43	7
30-34	27	5
35-39	36	7
40-44	31	12
45-49	32	13
50-54	17	6
55-64	26	15
65-74	15	2
75 and over	0	0
Unknown	91	23
TOTALS	421	131

Unusual forms

Information about symptoms and physical findings is based chiefly upon reports accompanying blood specimens submitted by physicians. In most cases, however, the description is brief and in many no clinical data are available. Clinical information has therefore been supplemented by personal observations by the senior author in a relatively small number of patients. From the data available it appears that the most frequently reported illnesses are similar to those described by Topping and associates⁴. In children, however, serious disease characterized by central nervous system symptoms or severe bleeding appears to be relatively common. In four children, 4 to 8 years old, there was severe bleeding from the nose and mouth and into

the gastro-intestinal tract and one of them, aged 4, died on the sixth day of illness. All had low hemoglobin and three children required blood transfusions. In two of these children there were also meningeal signs and one of these had an increase in the spinal fluid cell count. Three of these children had a generalized macular eruption and the fourth had petechiae. One child with a macular eruption also had some petechiae. In the fatal case, the chief findings were a faint generalized macular eruption, stiff neck, petechial eruption about the mouth, bleeding into the bowel, and a moderate increase in the spinal fluid cell count.

In five instances (a 46-year-old woman and four children, ages 6 to 9) there were marked symptoms and signs referable to the central nervous system. After onset with high fever, headache, and vomiting, patients were described as having some of the following findings: drowsy or stuporous, semicomatose, delirious, disoriented, irrational, mentally confused, and periods of restlessness or agitation. Stiff neck was mentioned as being present in one patient. Spinal puncture was attempted in four patients and was successful in three. In two patients there was a moderate increase in spinal fluid cell count with predominance of lymphocytes. Rash was observed in only one of these five patients. An eruption resembling that of measles but unaccompanied by fever was observed four days before onset of fever and central nervous system symptoms.

In an 8-year-old child the main findings were high fever, stiff neck and back, and an increase in cells in the spinal fluid. Data as to the duration of illness were available for nine of the 10 patients, the range being from six days in the fatal case to 17 days, most lasting from eight to 13 days.

In the severely ill patients a diagnosis of CTF was usually not suspected, apparently because descriptions of this disease have indicated a relatively benign dengue-like illness. Some blood specimens were sent in to exclude spotted fever because patients were seriously ill following tick bite. Virus was isolated from 55 children under the age of 10; thus 16 per cent (nine cases) had severe bleeding or serious symptoms referable to the central nervous system.

Discussion

Physicians in the U. S. generally recognize that an arthropod-transmitted virus such as the western equine encephalomyelitis virus may attack the central nervous system. They are less aware, however, that an arthropod-transmitted virus may affect the hemopoietic system and cause severe bleeding. Within recent years hemorrhagic phenomena have been reported to be due to members of the Russian spring-summer encephalitis group of viruses (Omsk hemorrhagic fever¹², Kyasanur Forest disease¹³, hemorrhagic fever in the Argentine¹⁴, and dengue fever virus¹⁵). Although up to the present time the number of cases of central nervous system and hemopoietic system syndromes which can be attributed to CTF virus has been small, clinicians in the Rocky Mountain area should be alert to their occurrence, especially in children under 10. Serious disease due to the

CTF virus may be more frequent than present data indicate.

Summary

Colorado tick fever virus has been isolated at the Rocky Mountain Laboratory from the blood of 552 patients. All these patients lived or visited in the Rocky Mountain area prior to their illness. Onset occurred between March 1 and October 14 and was most common during May and June. There were nine reports of serious illness with one fatal case. Four children had serious bleeding, four children and a 46-year-old woman had severe central nervous system symptoms suggesting acute encephalitis. One child with a milder illness had only a stiff neck and increased spinal fluid cell count. The real incidence of central nervous system involvement and severe bleeding in Colorado tick fever is unknown. ●

references on page 44



Ocular argyria

Roger C. Seyferth, D.D.S., M.D., Elko, Nevada

An unbelievable medical curiosity.

THE PATIENT IS AN 82-YEAR-OLD MALE seen with a complaint of dysuria. The most striking thing immediately noticeable about the patient was that his face resembled a grotesque Halloween mask and attention was, of course, directed to the eyes. He states that he sees fairly well, walks with a cane, and when asked how long his eyes have been black, he states "for years." The patient gives a history of having worked for 25 years in various lead and silver mines in Nevada. It has been about 20 years since he has done active mining. His eyes have been black for a number of years; he cannot remember how long. For the past two or three years he has been instilling drops in his eyes three times a day—Argyrol which he dilutes three to

one because this is more soothing. Nowhere else does this patient have any pigmentation in his body referable to or comparable with argyria.

Further ophthalmologic consultation was requested, and the following is submitted:

1. Visual acuity, uncorrected. Right eye: 20/100, left eye: 20/100.

2. External examination. The palpebral, bulbar and conjunctival fornices were all of a dark, black color. The cornea appears to be a dark, slate gray color. The iris is a pale greenish brown shade.

3. Slit lamp examination of the corneal endothelium shows a coarse, granular appearance and appears to have a dark gray mosaic pattern. This grainy appearance of the endothelium thickens toward the limbus, where it terminates. Both eyes show equal pigmentation of the endothelium. The epithelium showed two elliptical circumscribed areas located directly off center of the right eye. These areas show no corneal erosion, but rather black edges as if the edges had been drawn with black ink. The left eye

shows one area of this nature located slightly nasally. All of these areas are between two and three millimeters in diameter. The iris appears normal, although there is a slight atrophy of endothelium. The lens shows fine dust-like capacities in both eyes located within the nucleus.

4. Ophthalmoscopy. Ophthalmoscopic examination of both eyes shows macular degeneration. This degeneration appears to be a senile type. The area of involvement is four disc diameters in size, and circular. This is true in both eyes.

5. Spectacle correction. The best possible visual acuity is spectacle correction with a right eye 20/60 plus 1, and the left eye 20/50 plus 1.

This amiable gentleman appears to have no disability whatsoever referable to the argyria. This case is presented primarily as a medical curiosity, and it is interesting to know that, in spite of repeated cautioning, the patient still uses Argyrol drops and probably will continue to do so as long as the substance is available. •

Simple guides in the non-emergency treatment of diabetes mellitus



Jacobus H. Verhave, M.D., Portales, New Mexico

It is proper to rediscuss common problems of medical practice. Here is presented a plan for the treatment of patients with diabetes mellitus, based on methods that can be carried out easily in the home and office. Logically simple, this paper requires some degree of serious study.

A RELATIVE OR ABSOLUTE DEFICIENCY of insulin, regardless of its etiology, results in a chronic

disease called diabetes mellitus.

This lack of insulin causes a diminished utilization of glucose by body cells. As a consequence, the blood glucose level increases. At the same time, the kidney tubules, not able to reabsorb such a high concentration of glucose from the glomerular filtrate, will spill glucose in the urine. Both features, the hyperglycemia and the glycosuria, are the symptoms which raise the suspicion of diabetes mellitus. Neither one, however, is diagnostic of diabetes mellitus. It is well known that in a mild diabetic the fasting

blood sugar may be normal. On the other hand, a pronounced glycosuria may be a harmless renal abnormality, incorrectly termed "renal diabetes." This condition does not require any treatment at all.

Blood and urine sugar tests

The fasting blood sugar, the postprandial blood sugar and the measurements of reducing substance in the urine taken together are generally utilized in the diagnosis and treatment of diabetes mellitus. The blood sugar levels and the amount of "sugar" in the urine are reflections of the prescribed diet, the degree of physical activity and the antidiabetic drugs administered. Therefore the regulations of diet and medication can be determined in two ways. First by repeated examinations of the blood sugar to which there are sound objections. Second by the glucose content of the urine. The fasting blood sugar does not tell us anything about the blood sugar levels during the greater part of the day or night. Regulation of diabetics as controlled by blood sugar levels requires not only blood sugar determination at different daily intervals, but also requires a repeated daily blood sugar curve after every change of diet and/or insulin dosage. Not only are blood sugar determinations expensive, but they are inconvenient, uncomfortable and time-consuming. Glucose determinations of the urine in the regulation of diabetics are easier to carry out and, if executed correctly, are superior.

In elderly diabetics suffering from arteriosclerosis, hypertension and from chronic nephritis, the renal threshold is occasionally high. In these patients with high renal threshold having complications such as gangrene or infections, blood sugar determinations are indicated. Regulation of the diabetic primarily by the measurement of urinary glucose excretion is not new. However, the methods vary as regard the timing and the method of collection of the urine specimens. Joslin recommends testing the urine on arising and retiring, also before lunch and before dinner.

Nelson collects four specimens a day at 7:00 a.m. to 8:00 a.m., 11:30 a.m. to 12 noon, 5:00 p.m. to 6:00 p.m., and 7:00 p.m. to 9:00

p.m. He estimates the insulin dosage from qualitative determination. It is evident that isolated urinary glucose tests are not a reliable basis for calculating the insulin dosage during the different parts of the day. Sporadic glucose values are comparable to one picture taken from a fast moving film.

Cecil-Loeb recommends collecting all urine excreted during four consecutive periods extending over 24 hours. They advise that the specimen voided before each meal be included in the next collection. This confuses the end results, because those specimens voided before meals are secreted by the kidneys during the preceding period.

The four samples method

The method of the four samples, if correctly performed, gives a more accurate estimation of the insulin requirement during four periods of the day. This is true particularly if intermediate or long acting insulins are used. The urine should be collected by the patient as follows:

A. The *morning urine* (e.g., 8:00 a.m. to 12:00 noon). This portion occasionally contains glucose from the breakfast. It should contain all urine voided during the morning. It should not contain the urine voided on arising or before the prebreakfast injection or before breakfast. This morning period is terminated by emptying the bladder before lunch.

B. The *afternoon urine* (e.g., 12:00 noon to 6:00 p.m.). This portion occasionally contains glucose from the lunch. It should contain all urine voided during the afternoon, including the urine voided just before dinner.

C. The *evening urine* (e.g., 6:00 p.m. to 11:00 p.m.). This portion will occasionally contain glucose from the dinner. It should contain all urine voided during the evening. This period is terminated by emptying the bladder just before retiring.

D. The *night urine* (e.g., 11:00 p.m. to 8:00 a.m.). This portion should contain all urine voided during the night, to which the specimen voided just before breakfast is added.

The patient must measure the amount of urine contained in each of the four portions.

The quantitative determination using clinical test tablets or Benedict's reagent will reveal the amount of reducing substance spilled in each separate period. In certain cases it is advisable to divide the morning urine into two portions, i.e., 8:00 a.m. to 10:00 a.m., and 10:00 a.m. to 12:00 noon. The reason for this division will be discussed later on.

There is an increasing use of intermediate and long-acting insulins, known as lente insulins. An editorial in the *Lancet* regarding this tendency states: "There seem now to be good reasons to use the lente-preparations for all new cases of diabetes requiring insulin, so that globin-insulin, protamine-zinc insulin and N.P.H. insulin should gradually fall into disuse as new generations of diabetics grow up."

Lente insulin

This growing enthusiasm for the use of lente insulins is understandable, notwithstanding the availability of oral antidiabetic drugs. The reasons are as follows:

1. The onset of effect of protamine-zinc insulin is too slow (two hours), and its action too prolonged (30-36 hours). Globin insulin and N.P.H. insulin are intermediate insulins. Their time of action is too short (16-20 hours) to cover the need of insulin in many diabetics.

2. Oral antidiabetic drugs are relatively ineffective in the younger age group. In the 30 to 40-year age group 70 per cent are primary failures. Between the ages of 40 to 50, 50 per cent are primary failures. Between the ages of 50 and 60, 40 per cent are primary failures.

3. In a study of 200 patients receiving tolbutamide (orinase) and who were followed up to three years, the rate of secondary failure in drug response was 29.5 per cent. In the first year the rate of failure in the above group was 16 per cent. The monthly rate of secondary failures averaged about 3 per cent of the patients treated each month. Should this rate continue, all patients would eventually become resistant to tolbutamide. Once a patient fails to respond to the drug, the failure is permanent. However, he may respond (20 to 55 per cent) to an-

other oral hypoglycemic drug.

4. Oral hypoglycemic drugs are contraindicated in ketosis, precoma, diabetic coma, acute infectious conditions, trauma, operations, in pregnancy and in liver and kidney diseases.

5. Agranulocytosis after treatment with tolbutamide never has been proved. Oral antidiabetic drugs are broken down in the liver and excreted by the kidneys. Cases of severe hepatic damage have been recently published: The biguanides (D.B.I., D.B.B., D.B.V.) cause gastrointestinal side effects in a significant number of patients. Metahexamide (Melonex, Euglycin) have caused serious (and in some cases fatal) hepatic necrosis. Subsequently, metahexamide was withdrawn from clinical trial.

6. Without functioning beta-cells of the islands of Langerhans, the oral hypoglycemic drugs are ineffective.

Krall (Joslin Clinic) reviewed 350 patients, who received one or more doses of the biguanides (D.B.I., D.B.B., D.B.V.) between December 1956 and April 1959, and states: "None of the presently available oral hypoglycemic agents is completely adequate, and all seem to nibble at the periphery of lower blood sugar values rather than strike at the basic aspects of diabetes. There is even some question as to whether or not the diabetes or the blood sugar level is being treated. The era of the precise tool must not, for physicians, degenerate into an age of convenience, with an acceptance of lesser standards of treatment because of the convenience of oral therapy."

The variations in response of diabetics to a given dose of insulin requires that each patient's dosage should be adjusted according to his individual response. There are many variables which determine the individual reaction following insulin administration. Age, endogenous insulin production, nutritional state, emotional state, physical activity, even the blood circulation of the injection place, determine the final result of blood sugar level and glycosuria. Therefore it is not surprising that various investigators arrive at different findings for the onset, the maximum effect and the duration of action of lente insulins.

Summarizing the results in the literature we arrive at the following:

Type	Onset	Maximum effect	Duration
Regular insulin.....	20 min.	3- 4 hours	6- 8 hours
Semi-lente insulin	30 min.	6- 8 hours	12-14 hours
Lente insulin	45-60 min.	8-10 hours	16-20 hours
Ultra-lente insulin	2 hours	16-20 hours	24-30 hours

Applying the method of the four samples as described above, regulation of the diabetic with a proper dietary regime and with any kind of insulin is possible. The scope of this discussion will be limited to the use of the lente insulin preparations, known as "lente insulin," "semi-lente insulin," and "ultra-lente insulin." Lente insulin is a mixture of 30 per cent semi-lente insulin and 70 per cent ultra-lente insulin.

Glucose-equivalents

The "glucose-equivalent" is defined as the amount of glucose in grams metabolized from the urine by the administration of one unit of insulin. In other words, the amount of grams of glucose broken down to CO_2 and H_2O .

In mild diabetics the glucose-equivalent is $2\frac{1}{2}$ to 3. This figure decreases as the severity of the diabetic state increases. In infectious diseases and in acidosis the glucose-equivalent is less than 1. In coma it may drop to $1/10$.

There are the following possibilities:

1. The nonoverweight diabetic, following only the standard diet of 1,500 calories (150 gm. carbohydrate, 68 gm. fat, 72 gm. protein), and who spills less than 30 grams of glucose without acetonuria on the fourth to sixth day, requires an amount of $1/3n^*$ units of lente insulin before breakfast. This also applies to the obese diabetic, who follows a "standard diet," modified by a low fat content. In the above two examples the glucose-equivalent is 3, if the diabetic spills n grams of glucose in 24 hours. In the mild diabetic, especially the obese patient, it is possible to achieve aglycosuria solely by a dietary regime.

2. In case the diabetic who is on a standard diet, spills between 30 and 60 grams

of glucose, and also a small amount of acetone on the third to fourth day, $\frac{1}{2}n$ units of lente insulin should be given. In this case the glucose-equivalent, being 2, is less favorable.

3. A diabetic started on a standard diet and who spills more than 60 grams of glucose with moderate acetone should receive $\frac{3}{4}n$ units of lente insulin on the second or third day.

4. The diabetic who on the first day spills considerably more than 60 grams of glucose and who has a clear-cut acetonuria or diabetic acid in the urine should receive on the first day in units of regular insulin an amount equal to one-half to three-fourths of the amount of grams of carbohydrates in his diet. Because this amount will be more than 40 u. of regular insulin, the patient should receive his insulin divided into two or three injections, i.e., before meals and if necessary before retiring. In addition, the carbohydrates in the standard diet should be increased by 100 to 200 grams in order to suppress the ketosis. At the same time the diet should not be "ketogenic," i.e., low in fat and protein.

The lente insulins are contra-indicated in the treatment of precoma and diabetic coma. Regular insulin should be used. However, it is sometimes possible to continue the lente insulins and to give additional regular insulin whenever the glucose-equivalent drops during acute infections, trauma or operations.

Because the onset of lente insulin is slow, the breakfast should be taken one hour after the injection. It should be low in carbohydrates (20 to 30 grams). The carbohydrates of the lunch should vary between 40 to 50 grams.

Shifting insulin doses

Regarding the four samples, there are the following possibilities:

* n equals the amount of glucose in grams spilled into the urine in a 24-hour period.

1. If all four portions after lente insulin are positive, the dose should be increased (see preceding page).

2. If all four portions after lente insulin are negative, the dose should be decreased.

3. In the event that one or more portions are negative: a. If only the morning urine shows glycosuria after the lente insulin the ratio of semi-lente to ultra-lente (30:70) may be changed by increasing the semi-lente component. Another alternative is that of adding some semi-lente to the lente insulin. b. If the afternoon portion contains glucose after lente insulin, some of the carbohydrates from lunch may be shifted to breakfast. As another alternative, the ratio of semi-lente to ultra-lente may be changed by increasing the semi-lente. c. If the evening or night urine portion shows glycosuria after lente insulin, the ratio of semi-lente to ultra-lente may be changed by increasing the ultra-lente. Another alternative is that of adding some ultra-lente to the lente insulin.

In general it is possible to decrease the amount of carbohydrates of the meal preceding the glycosuria. This may be done by shifting some of these carbohydrates to another meal, which is itself followed by a period of aglycosuria. In other cases it is possible that by decreasing the amount of all carbohydrates, aglycosuria may result in all four urine samples. In the event of the occurrence of morning glycosuria, the above mentioned subdivision of the "morning urine" (secreted between 8:00 a.m. to 10:00 a.m., and 10:00 a.m. to 12:00 noon) will supply information indicating the period for which the prebreakfast injection failed. For instance, if the 8:00 a.m. to 10:00 a.m. portion is negative an overlapping effect of the ultra-lente component is possible. If the 10:00 a.m. to 12:00 noon urine mixture is strongly positive, the onset of effect of the semi-lente was probably too slow. On the other hand, if the 8:00 a.m. to 10:00 a.m. portion is positive an insufficient amount of ultra-lente may have been given. If the 10:00 a.m. to 12:00 noon mixture is negative (and at times associated

with hypoglycemia symptoms), too much semi-lente may have been given. In the event that there is hypoglycemia in the afternoon, the ratio of semi-lente to ultra-lente may be changed by decreasing the semi-lente. Also shifting some of the carbohydrates may prevent afternoon hypoglycemia. Stubborn morning glycosuria is sometimes prevented by administering regular insulin and lente insulin, provided that the regular insulin is drawn into the syringe first, with the lente insulin following. Regular insulin (pH 2.5 to 3.5) is more acid than lente insulin (pH 7.2). If lente insulin is drawn first followed by regular insulin, the ampule of regular insulin would receive traces of the alkaline lente insulin. This results in the formation of insulin crystals, which convert regular insulin into long acting insulin.

The advantages of the three lente insulins are:

a. A high percentage of diabetics can be regulated effectively with one injection a day.

b. Semi-lente, ultra-lente and lente insulin do not contain foreign protein, therefore local or general allergic reactions are less frequently seen.

Final instructions

No insulin, particularly the long acting insulins, should be prescribed for a patient without explaining the symptoms of beginning hypoglycemia. These are: "jitters," sudden perspiration, palpitations, hot flushes, anxiety, restlessness, pseudo-inebriation, aggressiveness, double vision and difficulty in speaking.

The patient should be cautioned to check each new vial of insulin to see if it is 40 units per cc. or 80 units per cc. This will prevent unexpected hypoglycemia.

Finally the physician should require his diabetic patient to carry at least five lumps of sugar at all times in order to suppress the first symptoms of an impending hypoglycemia. •

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Pyelonephritis*

John L. Emmett, M.D., Rochester, Minnesota

A renewed interest in this disease has led to fascinating concepts as to pathogenesis. Diagnosis can be overdone if bacteriuria is always thought to represent infection. Improper catheterization can be causative of infection. Treatment should be carefully planned.

THE PAST FIVE YEARS have seen a sharp resurgence of interest in pyelonephritis, which has stimulated fresh investigation into this comparatively neglected subject. Significantly, most of this investigative work has been done by internists and pathologists, and not by urologists. Not until these workers boldly asserted that the urethral catheter might be a prime causative factor in pyelonephritis did the urologists rub their eyes, sit up, and take notice.

Incidence

To emphasize the seriousness of the problem, it has been stated that (1) pyelonephritis is second only in frequency of occurrence to respiratory infections, (2) it is found in 6 to 20 per cent of all necropsies, although the diagnosis was made before death in only 20 per cent of such instances, (3) asymptomatic bacteriuria is present in 5 to 40 per cent of normal adults (more frequently in women than men) and may be the intermediary stage of fatal pyelonephritis and (4) the urethral catheter may be the cause of pyelo-

nephritis more often than is appreciated.

In a classic clinicopathologic study reported in 1940, Weiss and Parker¹ concluded that (1) pyelonephritis is more common than glomerulonephritis, (2) diffuse pyelonephritis in its chronic and healed stages should be considered as one form of Bright's disease, (3) pyelonephritis is responsible for 15 to 20 per cent of all cases of malignant hypertension and is more often the cause of small scarred contracted kidneys than is glomerulonephritis and (4) in some cases, vascular changes in the kidney considered to be degenerative and labeled "nephrosclerosis" are in reality proliferative changes resulting from pyelonephritis.

Mallory² also pointed up the role of pyelonephritis in malignant hypertension, stating that clinical malignant hypertension does not represent a single pathologic entity but may occur as the terminal phase of benign essential hypertension, chronic glomerulonephritis, or healed or chronic pyelonephritis.

However, investigators who think that the frequency and seriousness of pyelonephritis have been overemphasized point to the 1942 study of Bell³, who, reviewing 32,000 necropsies, found only 14 cases of chronic bilateral pyelonephritis in persons without demonstrable obstruction of the urinary tract; in the presence of gross urinary obstruction, however, the incidence was 12 times as great. He concluded that the majority of patients with acute pyelonephritis recover, a few die, and a few have chronic disease.

Pathogenesis

Probably the most important aspect of recent work has been animal experimentation concerning the manner in which the kidneys are infected. Is the mechanism hematogenous

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(descending) or urogenous (ascending) or neither? In evaluating this recent work, one should remember that 85 per cent of pyelonephritis in man is bacillary in origin, and it is impossible to produce bacillary pyelonephritis in animals by the intravenous injection of bacilli without first ligating the ureter.

Intrarenal hydronephrosis

In 1950, De Navasquez¹, working with rabbits, showed that, in contrast to the difficulty of producing bacillary pyelonephritis, it was easy to produce pyelonephritis by the intravenous injection of coagulase-positive *Staphylococcus aureus*, ureteral ligation not being necessary. His theory was that the coagulase produced by the bacteria diffuses through the arterioles into the surrounding parenchyma, causing zones of coagulative necrosis in which organisms can multiply in situ undisturbed by phagocytic activity. In most of his animals, the infected kidneys healed, with scars that could be seen on the renal surface. In 1956, De Navasquez² showed that, if staphylococcal pyelonephritis was first produced and then the kidney allowed to heal, the intravenous injection of colon bacilli would result in a bacillary pyelonephritis without the necessity of ligating the ureter. His explanation was that the scars resulting from healing produce tubular obstruction and stasis, leaving the kidney vulnerable to infection, just as it is when the ureter is obstructed. He called this tubular dilatation "intrarenal hydronephrosis."

As a result of these studies, De Navasquez postulated that the pathogenesis of chronic pyelonephritis in man is as follows:

1. Coccal pyelonephritis resulting from hematogenous infection with *Staph. aureus* secondary to some generalized disease, such as infections of the upper part of the respiratory tract, septicemia, exanthemas, furunculosis and abscessed teeth.
2. Healing, with formation of renal scars.
3. Resulting tubular obstruction (intrarenal hydronephrosis).
4. Recurring acute bacillary pyelonephritis.
5. Chronic pyelonephritis.

Beeson and associates³ confirmed the concept of De Navasquez regarding intrarenal hydronephrosis. They traumatized small lo-

calized zones in the kidney with a fine needle electrode. (More recently, they have been able to produce these lesions with a needle only, without fulguration.) Approximately seven days later, they injected colon bacilli intravenously into the animal. If the lesions were located either in the medulla or on a renal papilla, pyelonephritis developed within 48 hours; if they were in the cortex, pyelonephritis did not occur. They concluded that the lesions produce obstruction to tubular drainage, resulting in intrarenal hydronephrosis and stasis, with subsequent infection of the kidney. They also tried to produce ascending infection in these traumatized kidneys by introducing bacteria into the bladder three weeks after cautery; pyelonephritis occurred in three of eight cases. Calcification was noted in the obstructed, dilated, infected tubules in some animals which survived for a sufficient period. Thus, the healing of infected obstructed tubules in intrarenal hydronephrosis might be an etiologic factor in nephrocalcinosis in humans.

All the afore-mentioned data emphasize the importance of obstruction and stasis, whether microscopic or gross, as an etiologic factor in urinary infections.

Significance of bacteriuria

When does bacteriuria mean bona fide infection, and when does it represent only contamination from the urethra? The answer is obvious in a typical infection, with characteristic dysuria, fever, pyuria and bacilluria, but the distinction becomes of importance in the 5 to 40 per cent of normal adults who are said to have asymptomatic bacteriuria with little or no pyuria.

Previous studies by such workers as Schulte⁴ and Helmholz⁵ have demonstrated that "normal" male or female urethras harbor both pathogenic and nonpathogenic bacteria. Recent work by Guze and Beeson⁶, and by Monzon and associates¹⁰ has substantiated this finding. These last two groups of authors compared specimens of urine obtained by three methods, namely (1) needle aspiration through the bladder wall performed during abdominal operations, (2) urethral catheterization and (3) collection of a specimen during the middle of micturition. They found

that urine that was sterile when obtained by needle aspiration always showed bacteriuria in both catheterized specimens and those obtained at the midpoint of micturition. The number of bacterial colonies, however, usually was low, being less than 400 per milliliter. The count was less in the catheterized specimen than it was in the voided specimen.

Kass¹¹, as well as Sanford and associates¹², has shown that urethral contamination can be recognized by the quantitative study of cultures, concluding that counts of 100,000 or more bacteria per milliliter mean infection, while counts of less than 100,000 usually mean urethral contamination. Most clinical infections have bacterial counts of 1,000,000 to 10,000,000 organisms per milliliter. A few simple points in the technic of making quantitative cultures should be remembered. Cultures must be made within one hour, or else the specimen must be put in the refrigerator, because the common pathogens of the urinary tract multiply readily at room temperature, and the count easily may reach 10,000,000 per milliliter in 24 to 48 hours. Liquid culture mediums, such as broth, should not be used; it is better to make cultures from various dilutions of urine on pour plates of solid agar, after which the colonies can be counted.

Presence of pyuria

A simpler method of estimating the number of bacteria in urine is to do a gram stain of the uncentrifuged specimen. If bacteria can be found, the count is taken to be more than 100,000 per milliliter. Kass¹³ estimated this test to be 80 per cent accurate.

Another important question is whether bacteriuria occurs in the absence of pyuria and, if so, with what frequency. Some current investigators have stated that the error may reach 50 per cent if the presence of pyuria alone is used as an index of infection. This estimate appears too high to me. The figures of Sanford's group¹² apparently are more realistic; pyuria was absent in 13 of 91 cases of true bacteriuria (more than 100,000 organisms per milliliter) that they studied.

Thus, it may be concluded that both catheterized urine and specimens voided at mid-micturition are subject to urethral contamination, that contamination may be distinguished from true bacteriuria by quantitative

cultures or a gram stain of the uncentrifuged specimen, and that true infection may be present without pyuria in a relatively small number of cases.

Urethral catheter as etiologic factor

Much has been written recently concerning the dangers of urethral catheterization and its possible role in initiating pyelonephritis. One of the questions being asked most frequently concerns the risk of infection from catheterization. The risk varies with the situation and the reason for catheterization, but in every case it must be realized that pathogenic bacteria in the urethra can be pushed into the bladder with the tip of the catheter. In the presence of an indwelling catheter, the urine in the bladder becomes infected in 100 per cent of cases within four days regardless of whether or not prophylactic urinary antiseptics or antibiotics or both are used^{11,13}. Studies of series of cases in which a single diagnostic catheterization in women has been done in outpatient clinics under favorable conditions indicate that the incidence of post-catheterization infection varies from 2 to 4 per cent. If residual urine is present or if the patient has diabetes, the incidence is greater, of course.

Most urologists do not catheterize male patients simply to obtain a specimen of urine; instead, a midstream specimen obtained after cleansing the glans penis is employed. With proper equipment used by two nurses, or a physician and a nurse, in an office on a suitable treatment table, it should be possible by proper cleansing and separation of the labia to catch a satisfactory midstream specimen in women. Glaring examples of poor practice as far as catheterization is concerned are seen in hospitals. A typical situation involves an obese woman sunk deep in bed, poor light, and the most inexperienced nurse on the floor trying to accomplish a procedure that even the most experienced physician in the hospital could not do alone with sterile technic. Because the urethral meatus in the female is not easily seen even under the most favorable conditions, urethral catheterization of females in hospitals should be done by two nurses or one nurse and a physician.

Regardless of whether or not the catheter introduces infection, this instrument will

continue to be used. It has relieved many patients of painfully distended bladders and has saved many patients from uremic death. The problem is not one of whether the catheter should be used but rather of how to use it more efficiently. Prather and Sears¹⁴ compared the urethral catheter to the automobile, stating that people are killed daily in automobiles but yet they find the daily necessities and conveniences of the automobile sufficient to warrant its continued use on the basis that the benefits are greater than the dangers. In the patient without significant uropathy or associated diseases, such as diabetes, it is unlikely that a postcatheterization infection will lead to serious consequences, especially if it is recognized and promptly treated or, better yet, if prophylactic treatment is used. The implication is clear, however, that more attention should be paid to the technic of catheterization, and the catheter should be used with discrimination. I am not prepared to say whether properly obtained, midstream, voided specimens in women should be substituted for catheterized specimens for the purpose of diagnosis. Thus far, at the Mayo Clinic, my associates and I are still using catheterized specimens obtained under the most sterile conditions we can establish.

Classification

Articles in the current literature estimate that only 25 per cent of chronic urinary infections are controlled, the remaining 75 per cent being recurrent in nature. The rate of cure doubtlessly is low, but such figures are, of course, only guesses. For these data to be meaningful, some sort of classification of urinary infections should be made, and this is almost impossible.

About the best that can be done in classification is to divide infections into (1) those with underlying uropathy, such as stasis, stones and obstruction, or with associated contributory diseases, such as diabetes mellitus, and (2) those without demonstrable uropathy or associated disease. Also, one must distinguish between the occasional, simple, uncomplicated, acute infection that clears up rapidly either with or without treatment and the persistent chronic infection with recurring acute episodes that may

cause progressive renal deterioration. If the kidneys and ureters are normal by excretory urography in the presence of pyuria and bacteriuria, we are often not sure if the kidneys are infected and, if so, to what extent, or if the infection is confined to the bladder. At the clinic, we are doing ureteral catheterization to obtain specimens less and less, because nearly every cystoscopic examination is preceded by excretory urography. If the kidneys are urographically normal and if grossly clear urine is spurting from each ureteral orifice, examination of ureteral specimens of urine appears to be chiefly of academic importance, as it usually will not influence the method of treatment and only risk the introduction of infection into the kidneys from an infected bladder. Urologists should not think that ureteral catheterization is compulsory just because a cystoscope has been placed in the bladder.

Almost all of the acute infections and a large majority of the chronic infections are caused by gram-negative bacilli, chiefly *Escherichia coli* and *Aerobacter aerogenes*. However, the widespread use of antibiotics has greatly increased the relative incidence of *Proteus*, *Pseudomonas* and *Streptococcus faecalis* (enterococcus). The coagulase-positive type of *Staph. aureus* is a definite urinary pathogen, but opinions differ as to whether other staphylococci and streptococci found in the urine are of clinical importance.

Treatment

The question frequently is asked, especially by general practitioners, if it is acceptable practice to treat a urinary infection without first performing a complete urologic examination. I believe that such a preliminary trial of empiric treatment is justified if the physician is reasonably sure from the history and physical examination that gross or glaring uropathy is not present. For instance, in the preliminary survey, the physician's thinking should proceed somewhat as follows: If the patient is a child, does he have a constricted pin-point urethral meatus? The physician should watch him void; if a 6-year-old boy cannot urinate with a large forceful stream, investigation should be carried out. Is the bladder distended? If the child is anemic, renal insufficiency should be considered as a

possible cause. Excessive thirst and a low fixed specific gravity of the urine also suggest renal insufficiency. Enuresis or incontinence or both suggest uropathy that should be investigated. A mass in the flank may mean hydronephrosis or a renal tumor. If the patient is an adult, is the voiding free or is the bladder distended? Is the prostate enlarged or carcinomatous? Is a cystocele present? Has there been gross hematuria, suggesting a vesical tumor? Is a mass present in the flank? Is there anemia, suggesting uremia? Has there been colic, suggesting stone? Does the patient have diabetes?

If such a survey gives negative results, it is justifiable to institute treatment for a week or so without further urologic investigation. If infection persists at the end of this time or if it recurs, complete urologic investigation should be done before intensive treatment is begun.

Preliminary empiric treatment: Probably the most important consideration in instituting preliminary treatment is not to use antibiotics, because bacterial resistance to them develops so rapidly. Use of these agents should be postponed for a later all-out intensive attack. The reason for this is that one generally has only 10 to 20 days at most to use antibiotics effectively before resistant organisms appear. Resistant strains often emerge within a week, rendering the antibiotic impotent. The drugs of choice are the sulfonamides, nitrofurantoin (furadantin) and preparations of mandelic acid, all of which have a reasonably wide spectrum of activity and do not promote bacterial resistance.

The first choice usually is the sulfonamides because they are cheaper (on the basis of four tablets daily, the cost to the patient is \$1.50 per week for sulfonamides, \$12.00 for furadantin and \$15.00 for antibiotics) and because they are concentrated in both tissue and urine. Furadantin is concentrated only in the urine. It is still not entirely certain, however, just how important is the concentration of therapeutic agents in tissues in the treatment of urinary infection. Any of the newer sulfonamides, such as sulfisoxazole (gantrisin), sulfisomidine (elkosin) and sulfamethizole (thiosulfil), are satisfactory. All these agents are more soluble than is sulfa-

thiazole, and they rarely precipitate as crystals that block the renal tubules^{1,5}. They are also less toxic and show less acetylation to inactive forms. The recommended dose is usually 1 gm. given four times daily. In our experience, however, a dose of 0.5 gm. given four times daily is usually sufficient. Long-acting sulfonamides recently have been introduced. It is a distinct advantage to be able to prescribe only one 0.5-gm. tablet daily instead of one or two tablets four times per day, as with the conventional sulfonamides. Two long-acting drugs being used widely are sulfamethoxypyridazine (Kynex or Midicel) and sulfamethoxine (Madribon). They are excreted very slowly into the urine, so that high levels can be maintained in both blood and urine by a small dose given infrequently. These drugs should be used cautiously, however, because troublesome toxic reactions have been reported that have not yet been fully evaluated.

Method for increasing effectiveness

Furadantin is an excellent urinary antiseptic. Despite the fact that it does not concentrate in tissues, as already noted, it is often more effective than either sulfonamides or antibiotics. Also, as is true of sulfonamides, it does not cause resistance in bacteria. The average dose for an adult is usually 100 mg. given four times per day.

Mandelic acid is useful in milder urinary infections, especially if the offending organism is *Str. faecalis*. The most commonly used preparations at present are methenamine mandelate (mandelamine) and calcium mandelate. The dose of mandelamine is 0.5 to 2 gm. given four times daily, and that of calcium mandelate is 3 gm. given four times per day. For these drugs to work effectively, the pH of the urine should be 5.5 or less. The recent suggestion by Kass¹¹ that methionine be used for the purpose of urinary acidification has provided a method for increasing the effectiveness of these drugs. The sulfur in methionine is oxidized to sulfate, which is excreted in the urine, making it acid. Kass suggested a dose of 12 gm. per day, but clinical experience suggests that if more than 8 gm. is given per day, the patient complains of the odor of hydrogen sulfide about his person. Methionine* is inexpensive;

it should be given in divided doses two or three times daily.

Treatment, if successful, should not be terminated too soon or the infection may recur. It is best to continue treatment for five to 10 days after the urine becomes sterile. If treatment is unsuccessful or if the infection recurs after apparently successful treatment, a complete urologic examination should be performed before definitive and intensive treatment is begun.

Definitive (Intensive) Treatment: As mentioned previously, complete urologic examination should be done first to determine if any uropathy is present; if found, such conditions should be corrected surgically if possible. Gram's stain and cultures, if possible, should be done to identify the organism. Tests of the bacteria for sensitivity to various drugs and antibiotics may be helpful. As a minimum, the physician should know if the offending organisms are bacilli or cocci or both. The important thing, of course, is to have the stage set for a quick and intensive "knockout" campaign to destroy the bacteria before resistance to antibiotics can develop.

Aggressiveness in treatment not always justified

It is difficult, if not impossible, to present a standard plan of intensive treatment because of the great differences of opinions that exist and the multitude of drugs and antibiotics that are available. Hard and fast rules cannot be given. My colleagues and I in the Section of Urology at the clinic carry out intensive treatment more or less in accordance with the following general outline: If the patient is not febrile and if the infection is not a serious, immediate threat to life, we most likely would first use the sulfonamides, furadantin or mandelic acid, as already described for preliminary empiric treatment. The reason for this choice is that antibiotics have been disappointing in the treatment of urinary infections and because the incidence of infections resistant to antibiotics has increased substantially. If treatment with the nonantibiotics proves unsuc-

cessful and if the infection is bacillary in nature, we would try tetracycline in doses of 250 to 500 mg. given orally every six hours. If no response is evident, we then might combine it with furadantin or one of the sulfonamides. If still unsuccessful, we would fall back on the "essence of time," with intermittent medication every other week or for one week of each month for several months. In this case, however, we would revert to the nonantibiotics (furadantin or sulfonamides) because the long-term use of antibiotics usually accomplishes little more than the production of resistant strains of bacteria.

If the infection is of coccal origin and does not respond to the nonantibiotics, we would await the results of tests for sensitivity before prescribing antibiotics and then would use the specific antibiotic indicated. If this regimen is unsuccessful, we then would return to long-term intermittent therapy, using nonantibiotics, as already described for bacillary infections.

This plan may appear to echo a defeatist attitude or a lack of aggressiveness. However, after seeing many patients who have been treated previously for urinary infections, I believe that too heroic an effort usually has been made to eliminate a relatively unimportant urinary infection that has no particular urgency. Not only has the infection been made resistant to all the antibiotics but excessive risks of toxic reactions have been taken that were not justified under the circumstances. There are, of course, many instances in which aggressive and heroic treatment is indicated. In such situations, it is our custom at the clinic to enlist the help of the "Antibiotic Service."

Treatment by Antibiotic Service: The Antibiotic Service at the clinic is under the direction of internists whose responsibility is to care for serious and dangerous infections such as septicemia, pneumonia and meningitis. Thus, they tend to be aggressive in their attack. They emphasize the importance of distinguishing between "bactericidal" and "bacteriostatic" antibiotics. Table 1 (prepared by them) divides the commoner antibacterials into these two groups. With the exception of penicillin, all of the bactericidal agents are toxic, usually affecting the kidneys, the eighth cranial nerve or the central

*A satisfactory source of methionine is the Nutritional Biochemical Corporation, 21010 Miles Avenue, Cleveland 28, Ohio.

TABLE 1
So-called bactericidal and bacteriostatic agents

Bactericidal	Bacteriostatic
Pencillin	Tetracyclines
Streptomycin (or dihydrostreptomycin)	Chloramphenicol
Bacitracin	Erythromycin (ilotycin)
Neomycin	Novobiocin (albamyacin, cathomycin)
Polymyxin B (aerosporin)	Triacetyloleandomycin (cyclamycin)
Ristocetin (spontin)	Sulfonamides
Kanamycin	Nitrofurantoin
Vancomycin	Calcium mandelate
	Methionine

TABLE 2
Suggested initial antibiotic regimens for serious infections of the urinary tract

Antibiotic	Organism
Combined tetracycline and streptomycin	Coli-aerogenes group Proteus (novobiocin?) Pseudomonas (polymyxin B?) Paracolon group Salmonella (chloramphenicol?)
Combined penicillin and streptomycin	Enterococci (Str. faecalis)
Penicillin	Streptococcus pyogenes Streptococcus mitis
Antibiotic to be dictated by in vitro inhibition tests	Staphylococcus aureus (coagulase positive)

nervous system. Bacitracin, neomycin, polymyxin, kanamycin and vancomycin are especially dangerous in this regard and are best administered with the patient under observation in the hospital. Although streptomycin is given to outpatients, they must be watched carefully for tinnitus, loss of hearing and vertigo. All of the bactericidal drugs except penicillin must be given parenterally because they are not absorbed sufficiently with oral administration. Streptomycin, polymyxin, bacitracin, neomycin and kanamycin are given intramuscularly. Vancomycin and ristocetin must be given intravenously.

Table 2 summarizes the opinions of the

consultants on the Antibiotic Service concerning selection of various drugs and antibiotics for the *initial* treatment of various bacteria. In bacillary infections, regardless of which bacillus is present, they favor immediate treatment with a combination of streptomycin and tetracycline (0.5 to 1 gm. of streptomycin twice daily, and 500 to 750 mg. of tetracycline every six hours). Their reason for this approach is that (1) resistance develops rapidly to either antibiotic alone (more rapidly to streptomycin), but in combination each drug tends to prevent the development of resistance to the other, a theory that has been proved in the treatment of tuberculosis with streptomycin, para-aminosalicylic acid and isoniazid, and (2) they believe that a bactericidal agent such as streptomycin has a greater chance of eliminating the infection than has a bacteriostatic drug. They criticize the common urologic procedure of using tetracycline alone, stating that resistance develops so rapidly that this drug is probably no more effective than are the sulfonamides.

Furthermore, even though tests for sensitivity show bacilli that are resistant to either streptomycin or tetracycline or to both, they still favor the use of this combination first because they suspect that tests for sensitivity in bacillary infections may not be a true measure of antibiotic activity in vivo. When streptomycin is being used, they stress the importance of careful observation of the patient to avoid damage to the eighth cranial nerve, insisting that not more than 1 gm. twice a day for two weeks or 0.5 gm. twice a day for four weeks be given. Its use should be avoided in patients with any degree of renal impairment, because if the blood level reaches 25 to 30 micrograms per milliliter, damage to the eighth cranial nerve may ensue. As already noted, signs of toxicity, such as tinnitus, vertigo or diminution in hearing, must be closely watched for. In case of doubt, audiographic and caloric tests should be done. The American Academy of Ophthalmology and Otolaryngology recently advised that the use of dihydrostreptomycin be discontinued because of the high incidence of deafness.

If the initial effort with streptomycin and tetracycline fails and the seriousness of the infection warrants continued heroic effort,

the use of other antibiotics that have been found to be effective is considered; these include polymyxin for *Pseudomonas*, novobiocin for *Proteus*, and chloramphenicol for *Salmonella* (Table 2). If these fail, tests for sensitivity should be done with other antibiotics and any found suitable should be used. Any of the antibiotics, even those developed especially for cocci, might be effective for a particular strain of bacillus. It often requires considerable nicety and maturity in judgment to decide when an infection is serious enough to warrant continued aggressive treatment. If the seriousness of the infection indicates consultation, the urologist and general practitioner are usually wise to seek assistance from internists who are experts on antibiotic therapy.

If the infection is coccal rather than bacillary, our Antibiotic Service would proceed with treatment as indicated in Table 2. In the case of *Str. faecalis* (enterococcus), they prefer to begin treatment with a combination of streptomycin and penicillin. Large doses of penicillin (up to 6,000,000 units given intramuscularly each day or up to 10,000,000 units by continuous intravenous drip) are used. Such treatment has proved successful in septicemia caused by *Str. faecalis*.

When cultures of urine reveal various types of streptococci, one cannot be sure if the organism is pathogenic or nonpathogenic. Actually, streptococci do not play a particularly important role in most urinary infections. Penicillin is usually effective for streptococci, as they have not developed resistance to penicillin. A different problem is presented by the coagulase-positive *Staph. aureus*. The current seriousness of staphylococcal infections in hospitals is well known. This organism has become resistant to penicillin, tetracycline and most of the newer antibiotics that have been developed to control it. If *Staph. aureus* is the offending organism, it is the practice of our Antibiotic Service immediately to perform tests for sensitivity until an antibiotic is found that appears to be effective. The relatively nontoxic antibiotics that can be given orally, such as erythromycin, triacetyloleandomycin and novobiocin, are used if they are effective. If not, the more toxic ones, such as kanamycin, neomycin, vancomycin and ristocetin, must be given.

Bacitracin may be used occasionally as a "last resort." In mixed infections (bacillary and coccal), combinations of antibiotics may be used. For instance, if *Str. faecalis* and *Aerobacter aerogenes* are both present, one might use a combination of streptomycin, penicillin and tetracycline, the streptomycin and penicillin being effective against *Str. faecalis*, and the streptomycin and tetracycline being used for *A. aerogenes*.

Chloramphenicol is again being used rather widely. Beginning in 1952, its use was restricted because of several fatal toxic reactions resulting from suppression of bone marrow and aplastic anemia. Because of this limited use, many organisms, both bacilli and cocci, that are now resistant to tetracycline are susceptible to chloramphenicol. Also, organisms do not develop resistance to chloramphenicol as rapidly as they do to tetracycline. At the clinic, we are still using this drug sparingly and with caution because of the 20 cases of aplastic anemia seen at the clinic that were caused by this drug; 50 per cent were fatal. It should be given only when the risk appears to be justified, and one should avoid long periods of medication, which apparently are a definite factor in its toxic reactions.

Prophylaxis

It is now generally agreed that it is unwise to administer *antibiotics* to an uninfected patient either before, during or after operation to prevent infection. Such a procedure apparently only creates resistant strains of bacteria that may take the patient's life. On the other hand, the use of *nonantibiotics*, such as the sulfonamides and furadantin, to prevent urinary infection after such instrumentation as catheterization, cystoscopy and the passage of sounds, appears to be rational. Administration of one of these drugs beginning immediately after instrumentation and continued for five to seven days should provide a poor culture medium for organisms that might have been carried inadvertently from the urethra into the bladder by a catheter or an instrument.

Summary and conclusions

Current interest in and investigation of urinary infections and pyelonephritis have yielded some worthwhile information, espe-

cially in pathogenesis and pathology. These studies also have provided helpful information concerning the evaluation of urinary cultures and the correlation of bacteriuria and pyuria.

The frequency of asymptomatic bacteriuria apparently has been somewhat exaggerated, and its importance as an intermediate step in fatal pyelonephritis certainly has not been proved. Likewise, the dangers of the urethral catheter have been somewhat overstated. Nevertheless, it is timely to urge caution and respect for urethral catheterization and to avoid its indiscriminate use. More attention should be paid to the technic of urethral catheterization, especially in hospital practice.

The antibiotics should be used sparingly and with discrimination in urinary infections because of the rapid emergence of bacterial resistance. Nonantibiotics, such as the sulfonamides, nitrofurantoin and mandelic acid, should be given first, as they provide a wide antibacterial spectrum and do not produce bacterial resistance. Antibiotics should be used only when conditions are as favorable as possible for a definitive and intensive attack against the infection. The importance of urinary stasis, either gross or microscopic, must be kept in mind; if stasis can be satisfactorily corrected, infection often disappears without chemotherapy. •

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A new combo for Colorado State Medical Society Annual Session

The A.M.A. and the Colorado State Medical Society are joining forces early in October in Denver, combining the A.M.A.'s annual Congress on Occupational Health with the CSMS Annual Session. The meeting will begin on Sunday, October 1, at the Shirley Savoy Hotel in Denver, with the Society's House of Delegates convening in the afternoon. The Society's annual Stag Smoker will be held Monday evening, October 2, at the Shirley Savoy. The annual banquet for both groups will be held Tuesday evening, October 3, at the Brown Palace-West Hotel.

The CSMS scientific program will convene Monday, October 2, with the morning session devoted to a special program presented by four outstanding national figures in veterinary medicine, particularly in research fields on subjects directly related to the sometimes startling impact upon our medical practices of recent discoveries

in veterinary medicine. Dr. Mark L. Morris, now President-elect and who will be President of the American Veterinary Association, will preside over the morning program.

The afternoon program on October 2 will be presented by Colorado's own physicians. An excellent program is being anticipated.

The Brown Palace-West will be the location October 3 and 4 for the scientific program of both organizations, at which time industrial health and industrial accidents will be discussed, along with Wednesday afternoon's program of interest to all on Workmen's Compensation. Participants will include national speakers as well as outstanding speakers from Colorado.

Plan now to attend this joint meeting October 1-4 in Denver. Set aside these dates on your calendar and plan to be here.

Cardiac sounds and murmurs in children*

Clinical interpretation

Colin H. M. Walker, M.D., Denver

*All murmurs are important,
including the innocent ones.
Here is a detailed guide to help in
recognizing murmurs, particularly
the latter. Some of our previous
concepts have changed. Note the
changes and save this handy reference.*

CLINICAL INTERPRETATION OF CARDIAC SOUNDS and murmurs in the field of congenital heart disease has reached such a degree of accuracy that today many children with cardiac anomalies can be confidently referred for surgery without the diagnostic aid of cardiac catheterization or angiocardiography. It has only been, of course, with the aid of advanced tools of investigation that the present day accuracy has been achieved. It is the purpose of this paper to review the current understanding of sounds and murmurs, phonocardiographic illustrations of which may be found in the papers to which reference is made below.

Fourth heart sound

It is probably less confusing to start the description of the heart sounds with the last, fourth or atrial sound. In the normal course of events this sound is not audible with the

stethoscope but can be seen phonocardiographically. It is only when the pressure and flow relationships between the right atrium and the right ventricle are disturbed that to this inaudible sound is added the atrial component of the first heart sound. This latter is loud enough to hear, is early in timing, and thus forms the third element of the atrial or pre-systolic gallop rhythm.

First heart sound

Although physiologically the first heart sound is sometimes divided into four components, from the clinical and practical point of view it is divided into two. The splitting of this sound is almost certainly due to asynchronous closure of the mitral and tricuspid valves, in that order. The splitting is best heard at the lower end of the sternum and it is sometimes difficult to distinguish this from an early systolic ejection sound, an atrial sound and an atrial or pre-systolic murmur. Wide splitting is usually found in complete right bundle block, especially if there is also wide splitting of the second sound in the pulmonary area. The intensity of the first sound seems to be governed by the position of the valve cusps at the onset of the ventricular systole so that it is loud when the valve cusps are wide open at this time. This can happen in situations where there is prolonged ventricular filling from atrio-ventricular valve stenosis, or increased blood flow across the atrio-ventricular valve or to conduction changes causing a short PR interval. Diminished intensity of the first sound may be due to these factors in reverse or to poor

*Presented in January, 1959, to the General Practice Review session of the University of Colorado Medical Center. Dr. Walker is Instructor in Pediatrics and Director, Denver Area Rheumatic Fever Diagnostic Service.

conduction of heart sounds caused by emphysema or a thick chest wall. Any factor which diminishes myocardial force will also diminish the intensity of the heart sounds.

Second heart sound

The second heart sound is likewise principally caused by the closure of the aortic and pulmonary valves, in that order, and it is for this reason that the sound is split in the pulmonary area. In babies the physiologic tachycardia sometimes makes a splitting of the sound, even in the pulmonary area, difficult to detect. There is also a physiologic variation in the width of splitting of the second sound in the pulmonary area. This is directly related to the respiratory phase, the splitting becoming wider on inspiration due to increased negative pressure in the chest causing increased venous return to the right side of the heart and therefore a greater flow of blood out through the pulmonary valve, causing a slightly later closure of that valve. Fixity of this splitting is classically observed in atrial septal defects in which there is a fairly constant and increased flow across the pulmonary valve owing to the left to right shunt at the atrial level. This is a most valuable diagnostic sign.

Excessively wide splitting of the second sound in the pulmonary area may be due to both abnormally delayed closure of the pulmonary valve or to early closure of the aortic valve in situations where there is a low resistance to left ventricular emptying such as in mitral regurgitation. Conduction abnormalities, such as right bundle branch block, and prolonged emptying time of the right ventricle caused by pulmonary stenosis, will also cause wide splitting of this sound. The exact physiologic mechanisms of some of the above mentioned changes are still a subject of debate. In certain pathologic states the splitting is reversed, the pulmonary valve closing before the aortic, and in this situation the splitting becomes narrowed during inspiration. This is a useful sign in the diagnosis of complete left bundle branch block, aortic stenosis, and in a few cases with large left to right shunts, patent ductus arteriosus and systemic hypertension. This physical sign is not an easy one to detect clinically. In the normal course of events splitting is inaudible

in the aortic, tricuspid and mitral areas because the intensity of the pulmonary closure is not sufficient to transmit to these areas. If splitting is detected in these areas, particularly the mitral, this is strong indication that the pulmonary second sound is abnormally intense and is probably indicative of pulmonary hypertension. Diminution of the second or pulmonary component of this sound, or indeed its absence, indicates abnormal flow through the pulmonary valve with quiet closure such as is found in pulmonary valvular stenosis. Much the same can be said for increase or decrease in intensity of the aortic component where systemic hypertension and aortic valve stenosis are concerned. In young children the pulmonary second sound is invariably louder than the aortic, due probably to physiologic right-sided increase in pressure which gradually diminishes with age.

Third heart sound

The third heart sound is believed to be due to vibrations set up during ventricular filling at the time of left atrial contraction. In children this is a normal finding. As mentioned above, in reference to right atrial contraction, it is probably true to say that if left atrial contraction vibrations become audible, this is (as opposed to the vibrations of ventricular filling) an abnormal finding. Abnormal left atrial sounds are therefore found in systemic hypertension with left ventricular hypertrophy, in certain types of mitral valve disease, in constrictive pericarditis, and in congenital heart disease, causing right to left shunts. These factors create an increased resistance to left ventricular filling or increased flow in the left heart, thus causing atrial overactivity and a loud third heart sound. The distinction between this third heart sound and splitting of the second sound and an opening snap is sometimes difficult clinically.

Mitral and tricuspid opening snaps will not be considered in detail as these are rare in childhood, being most commonly associated with valvular stenosis. Occasionally tricuspid opening snap is detected in atrial septal defects. The snap is usually maximal internal to the apex in mitral valve disease and occurs at the end of, or just after, the second mitral sound.

Ejection clicks

Ejection sounds or clicks are high-pitched, early systolic sounds of a clicking character which are usually found in relation to dilatation of the aorta or pulmonary artery. This observation is sometimes made in the presence of pulmonary hypertension or with mild or moderate pulmonary valve stenosis. The aortic variety are seen in the presence of coarctation, aneurism, systemic hypertension, aortic stenosis and sometimes regurgitation. The ejection sounds are not, in fact, due to the opening of the valve cusps but to accentuated ejection vibrations. This ejection click is sometimes difficult to distinguish clinically from splitting of the first heart sound.

HEART MURMURS

From the point of view of the general practitioner, one of the most important aspects of auscultation is the recognition of the innocent murmur. There is no such thing as an entirely insignificant murmur. The murmur may not indicate organic or functional abnormality, but the fact that it is present has considerable importance for the patient, his family, or both. For this reason most emphasis concerning murmurs will be placed on the recognition of the innocent murmur.

Innocent murmurs

Of recent years innocent murmurs have been divided into four categories, determined mainly according to their point of maximum intensity, i.e., the apex, the pulmonary area, the left sternal border, and the cardiorespiratory murmur, usually heard around the apex but occasionally in other areas also.

It has now been agreed that the apical innocent murmur is a relatively rare finding. This does not mean that the innocent murmur is inaudible at the apex, but it does mean that the murmur is maximum at another point. As the apex has lost "popularity," the pulmonary area has gained, and it has been observed that as children grow older the innocent murmur changes from being a vibratory one most often heard at the lower left sternal border and becomes more frequently a blowing one heard best in the pulmonary area. The over-all incidence of innocent mur-

murs is somewhere in the region of 35 per cent of all normal children. Phonocardiographically, however, soft murmurs have been observed in almost 100 per cent of normal subjects, though from the practical standpoint the figure of about 35 per cent should be kept in mind. These murmurs are equally distributed between the two sexes.

There are some characteristics common to almost all innocent murmurs:

1. The murmur is soft. On a Grade I to VI basis it is seldom if ever louder than Grade III and is usually of Grade I or II.

2. The murmur is usually short and often mid-systolic in time.

3. The murmur varies with posture, usually becoming louder in the lying down position.

4. The murmur is usually intensified with exercise and emotion, contrary to previous belief.

The following characteristics are not so constant but often helpful in diagnosis:

1. Variability with respiration. The murmur becomes softer and may disappear during inspiration. This should be distinguished from the true cardiorespiratory murmur which is a soft, high-frequency murmur, the characteristics of which are like breath sounds and which has a distinct variation during the respiratory phase.

2. The character of the murmur is often "vibratory" in type. Many words have been used to describe this sound such as buzzing, squeaking, rasping, squirting, and so on. This character is usually the one found when the murmur is maximum in intensity at the lower left sternal border, whereas the innocent murmur in the pulmonary area is often of a more blowing character.

3. Conductivity. Again, contrary to previous opinion, it is now realized that many innocent murmurs are well conducted and if a murmur is heard throughout the whole precordium and even if it is transmitted across to the right side of the sternum and up into the neck, this does not necessarily indicate organic abnormality. In fact, it can be said that inability to localize the murmur to any specific area or difficulty in determining its point of maximum intensity is often good indication that this murmur has no organic basis.

Significant systolic murmurs

These murmurs have, for the sake of convenience and classification, been divided into the ejection type murmur and the regurgitant type murmur. The *ejection* murmurs such as those found in valvular stenosis are diamond shaped in outline, giving the auscultatory impression of reaching a maximum crescendo somewhere in the middle third of systole. It is often possible to determine that the murmur ceases shortly before the second sound. These murmurs are not infrequently associated with the ejection clicks mentioned above. The *regurgitant* systolic murmurs are pansystolic in time and are caused by a flow of blood from a chamber or vessel which is at a higher pressure than that into which the blood is flowing. This type of murmur is seen in atrio-ventricular valve incompetence or septal defects. The detection of murmur in the early phase of systole is important because it is sometimes only this observation which distinguishes these regurgitant murmurs from the louder innocent ones. In young children a systolic murmur only may be heard in cases of patent ductus arteriosus, though some believe that skilled auscultation can usually detect a carry-through of the murmur into early diastole in most cases.

Significant diastolic murmurs

With the exception of the diastolic element of a venous hum, there is no diastolic murmur which can be regarded as without significance. Even those which up until now have been regarded as "functional," such as the Graham Steell or Austin Flint murmurs, or the "flow murmur" at the apex, heard in cases of congenital heart disease with left to right shunt, they all indicate organic change either at the point at which they are heard or at some more distant point in the cardiovascular system. Diastolic murmurs are caused by:

1. Ventricular filling with large flow through a normal valve or possibly a normal flow through a damaged valve.
2. Regurgitation from incompetence of the aortic or pulmonary valves.
3. Atrial systole (pre-systolic murmurs).

The opening snap of bad mitral or tricuspid valves occurs in early diastole and it is

following this that the ventricular filling murmur is heard. It is usually a low frequency, rumbling type of murmur and not infrequently gives the impression of starting a little late in diastole. The duration of the murmur and not its intensity is now regarded as the best guide to the degree of valve narrowing. The "flow murmur" of left to right shunts, on the other hand, is a relatively short murmur, occurring immediately after the third heart sound. This same timing is observed in the transient diastolic murmur of acute rheumatic carditis. The regurgitant murmurs in children are similar to those observed in adults, i.e., aortic insufficiency is characterized by a long, high-pitched pansystolic murmur heard down the left sternal border. The murmur of atrial systole is produced by atrioventricular flow during ventricular diastole and is the direct result of atrial contraction ejecting blood into the ventricle and therefore has an ejection murmur outline (diamond shape).

Continuous murmurs

The commonest continuous murmur, as mentioned above, is the venous hum and this is usually detected to the right of the sternum and high up over the clavicle or in the neck. This is an entirely innocent murmur though it may be heard in association with other murmurs which in themselves have some significance. The next commonest cause is the patent ductus, and the Gibson machinery murmur does not require further description. These two murmurs form the greater part of a large group of murmurs of vascular origin which include those produced by anomalous veins, aorto-pulmonary septal defect, broncho-pulmonary anastomosis, aortic arch anomalies, large tortuous collateral vessels and arterio-venous aneurisms. The murmurs in the next group are purely cardiac in origin and these are usually complicated defects. The third group is that in which both cardiac and vascular elements are involved, such as perforation of the sinus of Valsalva into the right ventricle or connection between the coronary artery and this ventricle. The group of continuous murmurs of extra-cardiovascular origin includes Paget's disease of the rib, pregnancy and the lactating breast and are, of course, only observed in the adult. All the

others are, however, seen in children and with the exception of the venous hum, they are all of considerable significance.

Conclusion

In conclusion, it might be restated that a cardiac murmur, no matter how innocent it may prove to be, has considerable importance in the mind of the patient, his family, or both. It is the duty of physicians to provide an adequate explanation for the murmur or to reach a decision as to its benignity. If this is not possible, the parents should be reassured that nothing will be lost by delaying further investigation and clarification of this finding.

Patterns of Disease

Travelers' diarrhea, that all-too-common affliction of Americans abroad, is not only baffling to the tourists involved but to the medical world as well. According to the latest issue of *Patterns of Disease*, a Parke, Davis & Company publication for the medical profession, no definitive cause for this puzzling ailment has yet been found. Possible causes considered have been Shigella and Salmonella, bacteria responsible for most cases of diarrhea in the United States. But in a study of American tourists in Mexico it was found that the incidence of these and of other organisms cultured was "such that travelers' diarrhea could not be attributed to any one of them. Nor could parasites, such as ameba, Trichomonas, or Giardia, be incriminated in cases of diarrhea of travelers in

If this reassurance cannot in all fairness be given, then it is advisable for everyone's peace of mind to seek further opinion and possibly request more detailed investigation. It is surely a greater error to diagnose cardiovascular abnormality in the presence of a normal cardiovascular system than it is to call the abnormal heart normal. If this attitude of mind prevails, much unnecessary suffering and worry can be avoided. •

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Europe." *Patterns* suggests that further study of the role of viruses and staphylococcus toxin may throw some light on the mystery of the ailment.

Colorado tick fever cont. from page 25

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- ¹⁵Hammon, W. McD.; Rudnick, A.; Sather, G. E.; Rogers, K. D.; La Motte, L. C., Jr.; Chan, V., and Dizon, J. J.: Philippine Hemorrhagic Fever, Etiological Relationship to Dengue. In press. (See book *Viral and Rickettsial Infections of Man*, 3d Edition, p. 372.)

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THE WASHINGTON SCENE

A monthly news summary from the nation's capital by the Washington Office of the A.M.A.

The American Medical Association branded as untrue certain statements by Abraham Ribicoff, Secretary of Health, Education and Welfare, concerning the Administration's legislative proposal to provide medical care for the aged under Social Security.

Dr. F. J. L. Blasingame, A.M.A. Executive Vice President, presented a point-by-point rebuttal in a letter to the more than 500 editors from throughout the country after Ribicoff addressed the annual meeting of the American Society of Newspaper Editors in Washington.

Dr. Edward R. Annis, Miami surgeon representing the A.M.A., accused Ribicoff of misrepresenting the role of doctors under the administration proposal. Dr. Annis answered Ribicoff on a radio-television program with Sen. Kenneth B. Keating (R., N. Y.) which was taped in Washington. Ribicoff had made the misrepresentation on an earlier Keating program.

Dr. Blasingame said Ribicoff's statement before

the editors that physicians are not included in the administration proposal, the King bill, "simply is not true." The A.M.A. official pointed out that the bill includes interns and residents in teaching hospitals as well as pathologists, radiologists, physiatrists and anesthesiologists working in hospitals or serving hospitals' outpatient clinics.

"Mr. Ribicoff further claims that the King bill provides free choice of hospital physician," Dr. Blasingame said. "The fact is only hospitals signing contracts with the federal government would be available to patients. If the only hospital in a community was not approved by the Secretary of HEW, patients in that community would be forced to seek hospitalization in some other city. That would not afford free choice of hospital. If the patient's physician was not on the staff of the other hospital, the patient would be denied free choice of physician."

Dr. Blasingame also disputed Ribicoff's contention that the King bill is not socialized medicine.

"By common definition, any scheme which calls for a system of compulsory health care which is administered, financed, and controlled by the federal government is socialized medicine for that segment of the population it serves."

Rep. Walter H. Judd (R., Minn.), who is a physician, was quoted as one of a number of House and Senate members who agree with the A.M.A.: "The public has been led to believe that they can get government financing without government

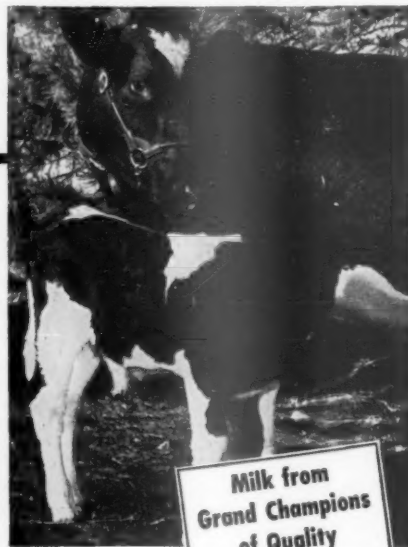
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control and ultimate government operation of medical services. It is naive for anyone to believe that Congress will take the people's money away from them through taxes and then allow the money to be spent by someone else without the Congress maintaining its own firm control."

Pointing out that the nation's physicians always have been in favor of medical care for all regardless of ability to pay, Dr. Blasingame said:

"It seems strange to us that Mr. Ribicoff continues to lobby for the King bill while completely ignoring the Kerr-Mills law, passed by Congress last year with strong support by the nation's physicians.

"The Kerr-Mills Law enables the states to guarantee to every aged American who needs help the health care he requires. And the states are implementing the law with unprecedented swiftness."

Dr. Annis pointed out on the radio-television program that "doctors would work for the government by working for the hospitals under contract to the government." He said that those doctors would work "under rules, regulations and controls prescribed and laid down" by the HEW.

Krebiozen evaluation

The Department of Health, Education and Welfare has agreed to make an impartial evaluation of the controversial cancer drug Krebiozen.

U. S. District Judge Julius H. Miner of Chicago requested the evaluation before proceeding with a \$300,000 libel suit filed by Andrew C. Ivy, M.D., a leading endorser of the drug, against George D. Stoddard, Ph.D., Chancellor of New York University and former President of the University of Illinois.

In a letter to HEW Secretary Ribicoff, Miner said:

"In my humble judgment, Krebiozen has too long been a controversial subject and the American public deserves that it be examined under neutral supervision and by the most competent experts in whom the people have implicit confidence."

Ribicoff said the National Cancer Institute would evaluate the drug when its sponsors presented the necessary data. But, he said, "any decision to undertake a study with human cancer patients must await, and depend on, the results of the evaluation of the existing clinical data."

Physicians' retirement

A new bill to encourage physicians and other self-employed persons to set up their own retirement plans started through Congress with approval of the House Ways and Means Committee.

Bearing the same number, H.R. 10, as a similar bill which died in Congress last year, the new measure would permit a self-employed person to defer taxes on income placed in a private retirement program. The special treatment would be

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limited to \$2,500 or 10 per cent of income each year, whichever is smaller.

Such income could be invested in qualified pension trusts, annuity programs, profit-sharing plans or a new type of nontransferable government bonds redeemable when the individual reaches retirement age or suffers disability.

An individual could start drawing benefits at age 59½, or earlier in the case of disability. A self-employed person would have to start drawing benefits by age 70½.

If a self-employed individual had more than three employees, he would be required to set up pension plans for them before he could benefit himself.



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Lanesta Gel has complete esthetic acceptance and is well tolerated.

*Gamble, C.J.: *Am. Pract. & Digest. Treat.* 11:852 (Oct.) 1960. See also Berberian, D.A., and Slichter, R.G.: *J.A.M.A.* 168:2257 (Dec. 27) 1958; Kaufman, S.A.: *Obst. and Gynec.* 15:401 (March) 1960; Warner, M.P.: *J.Am.M. Women's A.* 14:412 (May) 1959.

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“nutrition...present as a modifying or complicating factor in nearly every illness or disease state”¹

1. Youmans, J. B.: *Am. J. Med.* 25:659 (Nov.) 1958

cardiac diseases “Who can say, for example, whether the patient chronically ill with myocardial failure may not have a poorer myocardium because of a moderate deficiency in the vitamin B-complex? Something is known of the relationship of vitamin C to the intercellular ground substance and repair of tissues. One may speculate upon the effects of a deficiency of this vitamin, short of scurvy, upon the tissues in chronic disease.”²

2. Kampmeier, R. H.: *Am. J. Med.* 25:662 (Nov.) 1958.

arthritis “It is our practice to prescribe a multiple vitamin preparation to patients with rheumatoid arthritis simply to insure nutritional adequacy . . .”³

3. Fernandez-Herlihy, L.: *Lahey Clinic Bull.* 11:12 (July-Sept.) 1958.

digestive diseases Symptoms attributable to B-vitamin deficiency are commonly observed in patients on peptic ulcer diets.⁴ Daily administration of therapeutic vitamins to patients with hepatitis and cirrhosis is recommended by the National Research Council.⁵

4. Sebrell, W. H.: *Am. J. Med.* 25:673 (Nov.) 1958. 5. Pollack, H., and Halpern, S. L.: *Therapeutic Nutrition*. National Academy of Sciences and National Research Council, Washington, D. C., 1952, p. 57.

degenerative diseases “Studies by Wexberg, Jolliffe and others have indicated that many of the symptoms attributed in the past to senility or to cerebral arteriosclerosis seem to respond with remarkable speed to the administration of vitamins, particularly niacin and ascorbic acid. These facts indicate that the vitamin reserve of aging persons is lowered, even to the danger point, more than is the case in the average American adult.”⁶

6. Overholser, W., and Fong, T. C. C. In Stieglitz, E. J.: *Geriatric Medicine*, 3rd edition, J. B. Lippincott, Philadelphia, 1954, p. 264.

infectious diseases Infections cause a lowering of ascorbic acid levels in the plasma; and the absorption of this vitamin is reduced in diarrheal states.⁷

7. Goldsmith, G. A.: *Conference on Vitamin C*. The New York Academy of Sciences, New York City, Oct. 7 and 8, 1960. Reported in: *Medical Science* 8:772 (Dec.10) 1960.

diabetes Diabetics, like all patients on restricted diets, require an extra source of vitamins.⁸ “Rigidly limiting the bread intake of the diabetic patient automatically eliminates a large amount of thiamin from the diet. . . . There is some evidence of interference with normal riboflavin utilization during catabolic episodes.”⁹

8. Duncan, G. G.: *Diseases of Metabolism* 4th edition W. B. Saunders, Philadelphia, 1959, p. 812. 9. Pollack, H.: *Am. J. Med.* 25:708 (Nov.) 1958.

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15th Annual Rocky Mountain Cancer Conference

Brown Palace-West Hotel

Denver

July 12-13, 1961



Tuesday, July 11

2:00-5:00 p.m.—Advance registration

Wednesday, July 12

Morning

8:30 a.m.—Registration

9:00 a.m.—**WELCOME**—Cyrus W. Anderson, M.D., President, Colorado State Medical Society; Lanning E. Likes, M.D., President, Colorado Division, American Cancer Society; John Cline, M.D., President, American Cancer Society.

Introductions by Dr. Lanning E. Likes

9:30 a.m.—**SYMPOSIUM: "DETECT CANCER IN TIME!—PROCEDURES, PROBLEMS AND SOLUTIONS"**

Moderator: Kenneth C. Sawyer, M.D.

Participants: U. R. Bryner, M.D., William Dock, M.D., John R. McDonald, M.D., John W. Cline, M.D., Vincent P. Collins, M.D., John A. Wall, M.D.

10:30-10:50 a.m.—Coffee break

10:50-11:30 a.m.—Symposium continued

11:30-12:00 a.m.—Question and answer period

12:00 noon—Round Table Luncheon

Presiding: Ervin A. Hinds, M.D.



Ulrich R. Bryner, M.D.
Salt Lake City, Utah



John W. Cline, M.D.
San Francisco, California



Vincent P. Collins, M.D.
Houston, Texas



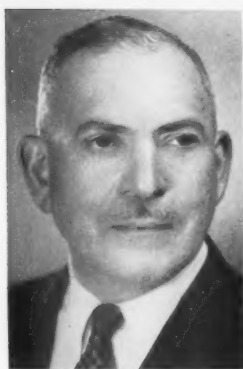
William Dock, M.D.
Brooklyn, New York

GUEST SPEAKERS

GUEST SPEAKERS



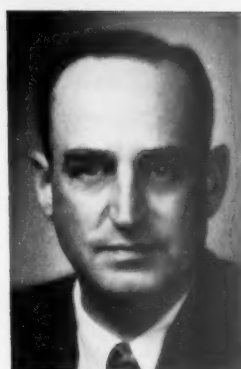
Leonard W. Larson, M.D.
Bismarck, North Dakota



Manuel E. Lichtenstein, M.D.
Chicago, Illinois



John R. McDonald, M.D.
Detroit, Michigan



John A. Wall, M.D.
Houston, Texas

Wednesday, July 12

Afternoon

Presiding: V. V. Anderson, M.D., President-elect, Colorado State Medical Society

2:00-2:30 p.m.—"General Practitioner's Role in Cancer Detection," U. R. Bryner, M.D.

2:30-3:00 p.m.—"Colostomy," Manuel E. Lichtenstein, M.D.

3:00-3:15 p.m.—Coffee break

3:15-3:45 p.m.—"Peptic Ulcer-Gastric Cancer Problem," William Dock, M.D.

3:45-4:15 p.m.—"Problems of Improving Cancer Detection in the Lung," John R. McDonald, M.D.

5:30-7:30 p.m.—Social Hour—Cash Bar and Snacks. This will be your opportunity to meet and chat with your guest speakers.

Thursday, July 13

Morning

8:00-12:00 a.m.—Registration

9:00 a.m.—**GREETINGS** from the American Medical Association, Leonard W. Larson, M.D., President

Introduction by V. V. Anderson, M.D., President-elect, Colorado State Medical Society

9:30 a.m.—**SYMPOSIUM: "NEOPLASMS OF THE FEMALE GENITAL TRACT"**

Moderator: N. Paul Isbell, M.D.

Participants: Manuel E. Lichtenstein, M.D., John R. McDonald, M.D., Vincent P. Collins, M.D., John A. Wall, M.D.

10:30-10:50 a.m.—Coffee break

10:50-11:30 a.m.—Symposium continued

11:30-12:00 a.m.—Question and answer period

12:00 noon—Round Table Luncheon

Presiding: Alexis E. Lubchenco, M.D.

Afternoon

Presiding: Myron C. Waddell, M.D.

2:00-2:30 p.m.—"Incipient Uterine Cancer—Diagnosis and Treatment," John A. Wall, M.D.

2:30-3:00 p.m.—"Duration of Cancer Before Diagnosis," Vincent P. Collins, M.D.

3:00-3:30 p.m.—Maytag Fellowship Lectures

Norman Welch, M.D., Pathology

James W. Thorpen, M.D., Pathology

William K. Magnum, M.D., Surgery

J. F. Prinzing, M.D., Surgery



ORGANIZATION



COLORADO

CU regents appoint Denver doctor

Dr. William Rhoads Waddell, 42, of the Harvard Medical School Thursday, May 4, was appointed Professor and Chairman of the Department of Surgery at the University of Colorado School of Medicine, effective May 15.

He will succeed Dr. Henry Swan, who resigned recently. The appointment was approved at a meeting of the CU Board of Regents on recommendation of Dr. Robert J. Glaser, CU Vice President for Medical Affairs and Dean of the School of Medicine, and the Executive Committee of the medical faculty.

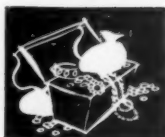
Obituary

Untimely death of CU researchist

David M. Gould, professor and chairman of the Department of Radiology at the University of Colorado School of Medicine, died April 2, 1961, at Colorado General Hospital from effects of a heart attack. Dr. Gould was born in Worcester, Massachusetts, on January 29, 1914, and received his Bachelor of Arts degree in 1935 from Clark University in Worcester. His medical degree came from Harvard Medical School in 1939 and his residency in radiology was at Johns Hopkins Hospital at Baltimore, Maryland. He then became a member of the faculty of Johns Hopkins Medical School until he went to Little Rock, Arkansas, where he was associated in radiology with the University of Arkansas Medical Center. He was licensed in Arkansas in 1956.

Dr. Gould joined the Colorado Medical School in September, 1959, and became head of the radiology department. His license to practice medicine in Colorado became effective in 1960.

Dr. Gould was a former President of the Association of University Radiologists and won prominence in research into metabolic bone diseases. He wrote a book on the subject of diagnostic radiology. Survivors include his wife and three sons.



MONTANA

Montana Chapter AAGP meets

Meeting of the Montana Chapter of the American Academy of General Practice will be held Friday and Saturday, June 16 and 17, at the Stagecoach Inn, West Yellowstone, Montana.

Participants for the two-day program include: M. Eugene Lahey, M.D., C. B. McVay, M.D., Vincent P. Collins, M.D., and David B. Cheek, M.D.

Nonmember registration \$5.00. AAGP Category 1, 8-10 credits.



NEW MEXICO

Dr. Omar Legant elected Fellow

Dr. Omar Legant, Vice Speaker of the House of Delegates and Past President of the Bernalillo County Medical Association, has received the honor of election to Fellowship in the American College of Radiology. This honor, bestowed by the College of Radiology, is in recognition of outstanding achievement and contribution to the art and science of medicine in general and radiology in particular.

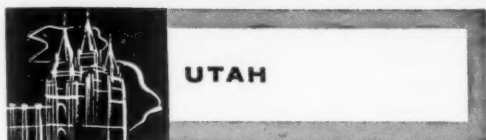
Investiture into Fellowship was made on Friday, February 10, 1961, at the Drake Hotel in Chicago as a highlight of the College Annual Meeting and Conference of Teachers of Clinical Radiology.

Announcement

Fourth Annual Ruidoso Clinics, July 17 through July 20, 1961, Ruidoso, N. M. Sponsored by the New Mexico Chapter, American Academy of General Practice.

Faculty: University of Texas Medical School, Galveston, Texas. Credit: Approximately 14 hours, Category I. Preregistration, \$25.00.

For information, write to Dr. R. W. Briggs, 406 N. Pennsylvania Ave., Roswell, New Mexico.



Salt Lake City doctor honored

Dr. C. H. Hardin Branch, Professor and head of the Department of Psychiatry, University of Utah College of Medicine, Salt Lake City, is the incoming President-elect of the American Psychiatric Association, it has been announced at APA's Annual Meeting in Chicago.

Construction to begin on Medical Center

A financial hurdle has been overcome and construction of the University of Utah Medical Center will begin within the year. The state has called for immediate bids for the \$10 million project.

The new center, which will be built in the northeast section of the University campus, will provide research laboratories, out-patient clinics, a medical library, a 200-bed teaching and research hospital and other facilities.

Construction is expected to begin around the first of July with completion hoped for by the fall of 1963 or early 1964.

A.M.A. holds Rural Health Conference

The American Medical Association held its second Regional Rural Health Conference in Salt Lake City, Utah, May 5 and 6. The conference, sponsored by the A.M.A.'s Council on Rural Health, centered around the theme "Community Resources for Health." It was under the direction of Dr. Fred A. Humphreys, Chairman of the Council.

Speakers included Dr. Alfred M. Popma, Boise, Idaho, Chairman of the Western Interstate Commission on Higher Education; Lloyd Sommerville, Grand Junction, Colorado, President of the Colorado Farm Bureau; Cyrus W. Anderson, M.D., Denver, Colorado, President of the Colorado State Medical Society; Franklin H. Top, M.D., Professor and Head of the Department of Hygiene and Preventive Medicine as well as Director, Institute of Agricultural Medicine, State University of Iowa.

Proceedings of the House of Delegates Utah State Medical Association

Fourth Interim Meeting
Salt Lake City, Utah
March 11, 1961

The Fourth Interim Meeting of the House of Delegates of the Utah State Medical Association convened at 9:00 a.m. March 11 in the Little

Theatre, University of Utah, Salt Lake City. Following are the discussions and actions taken.

Speaker R. N. Hirst: First on our agenda today is approval of the minutes of the 1960 Annual Session of the House of Delegates as published in the Rocky Mountain Medical Journal. (Approved)

Speaker Hirst then called upon President Brooke.

President's report

President Brooke: Mr. Speaker and fellow Delegates, we are meeting today in what I hope will be a short and yet productive meeting of the minds to further delineate the problems which we have constantly in all such associations as ours.

I might recount a few of them for you, to tell you not that we have solved a lot of these things, but to acquaint you with a well known fact and to have you think about it too that a lot of these things recur year after year, seemingly at times in a nauseating fashion but because of the constant need for reviewing certain policies that we have, for the constant need in any democratic association for acquainting everybody concerned with just why things have been done in the past and why things might have to be changed in the future.

This, of course, refers to such things as meetings that we have and have had over the years, increasingly more so recently with Labor. Your association meets at least once a year on a state level with leaders of Labor associations who are more and more entering into contracts and attempts in one way or another to secure fringe benefits and therefore to set fees. We meet also with pharmacists and members of their associations once every year. We have had and will continue to have, I hope, a meeting with the legal profession in which the medical-legal problems are brought out every year in panel form.

We have a press-radio meeting once a year in which we review the press-radio code as it applies to announcements by physicians over our media of expression and we also at this time, of course, award to the doctor in the state that we some token or recognition.

We have been interested this year in a high school entrance program and under the chairmanship of Dr. Critchfield we have attempted to increase interest by those doctors who are taking care of high school athletic programs; increase interest in their cooperation with coaches in the prevention of injuries in the discussion of such things as common types of football, basketball and track injuries and next week at BYU is a full-day meeting of those members of our profession who have been contributing so well to the care of our high school sons and primarily in the high schools, a little junior high of course, but contributing to their health in the prevention of serious injuries.

Another recurring problem and one that I am

afraid we are not doing too well with, but it is natural in certain ways because of inertia and because of the fact that we really haven't been hit with any catastrophe, and that is the so-called problem of civil defense, which includes the bombing aspect but also the mass injuries of any catastrophe of a civilian sort. To get this started, there was a program at Camp Williams with the Army and this has been set up to get things going. A hospital, of which there are now a good many of them available for catastrophes in Utah—one of these hospitals was set up at Camp Williams and is there for inspection.

In addition to that, under Dr. Paul Keller, who is Chairman, we have inaugurated the first attempts at training para-medical people, dentists and veterinarians and nurses, all sorts of people who might have to have a much greater share in the care of injuries in any real disaster.

It is hoped that after this meeting is carried through this winter and spring, that other hospitals will take up the same training program and carry it forth.

On our legislation, in this present session of the Utah Legislature, we have been successful. The Basic Science Amendment was passed yesterday and the Mental Health Bill went through.

Our Good Samaritan Law, which was a very short thing but prevents the usual type of suit against the doctor who stops at a roadside accident, prevents this suit in the sense that he can't be charged with the usual grounds of abandonment and negligence and so forth. This was modeled after California's law and went through.

\$1,250,000.00 was passed by the Legislature to be matched doubly by the federal people to the extent that Utah would get, as I understand, \$3,750,000.00 under the Kerr-Mills Bill. This is not enough, of course, for a full program but it is a start and does get us on the road with this mechanism of payment in contrast to the social security type.

Now we need a lot of things that haven't come to pass. We need a review and revision of the fee has been most public-spirited, a plaque or Medical Licensing Act which has not been changed since 1919 or thereabouts, as it applies to doctors who want to apply in our state. We need consideration of whether this should be changed to allow certain kind of foreign graduates to practice in this state. I am not necessarily advocating that they be, but any law that hasn't been revised for this length of time certainly needs consideration. As I understand it, we are one of the six states who, under no circumstances, allow any graduate of a medical school abroad, whether he be a citizen or not, to practice here. This is a complex problem. If we did anything like this, we would have to draw up some pretty tight restrictions to prevent the things we all know might happen.

The Grievance Committee situation in the state

I think should be changed. A resolution has been introduced to be referred to a reference committee on this regard. It's patently and obviously sort of unworkable, I think, to require that in a small county society, and some of our county societies have no great number of doctors, it is unwise to ask them to sit as a judgment board to discipline a member with whom they practice in a small community. Even if it isn't unfair, it would seem sort of bad that if they did discipline, they might be accused—and rightly—as benefiting by any such discipline. Therefore, our Constitution and By-Laws Committee, headed by Dr. Morgan Coombs, is attempting to get some changes in this Grievance Committee system which would allow this type of judgment to be done by the people who would not be accused of benefiting by any such judgment.

We hope to have this as a Constitution and By-Laws change up for your consideration in the next September meeting.

One thing that I am agreed that we are going to have a little trouble with is the question of ethics and this implies consideration of possible review of the procedures used by federal and state governments when they set up panels of physicians for use in the federal industrial program. For instance, crippled children, for any number of things that might come in on the state or federal level where panels of physicians are appointed. We would like to be sure as the Council would, I am sure you all would, that these panels aren't appointed in a capricious or arbitrary manner; that it is done—allowing everybody a chance at this and that we are cooperating in the setup of these panels. I think you would all want that and not want it to be established by a small clique of people.

In addition to this we need to consider the ethics of when it is and when it is not desirable for doctors to tour the state as specialists for health. I don't think it is any wish of any of us to curtail initiative.

Inasmuch as ethics can guide anything—we are not attempting to be compulsory, at least I don't feel so, but we do—I think all of us would like some sort of ethical guide as to when it is right and when it is wrong to do this. Thank you.

Speaker Hirst: Now the report of the Secretary.

Secretary's report

Dr. John Waldo: The report of the Secretary is essentially the report of the Scientific Program Committee.

This committee has met now on a number of occasions and we have had a considerable flow of correspondence with the result that our scientific meeting for September is well into the stages of being finalized and we hope within a month our entire program will be set and ready for distribution at the proper time.

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References: 1. Smigel, J. O., et al.: J. Am. Geriatrics Soc. 7:61 (Jan.) 1959. 2. Shalowitz, M.: Geriatrics 11:312 (July) 1956.

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Report of the Fee Schedule Committee

Dr. Homer Smith: It had been our original hope that at this time we could present to you a final version of the new relative index value study that we have been undertaking during these past two years but the formidable past does not lend itself to a conclusion at this time so I am going to read to you a report that I had not sent in for publication.

The Fee Schedule Committee of the Utah State Medical Association has been meeting for the past two years to endeavor to develop a relative value index pertaining to the services rendered by the physicians and surgeons of Utah. It should be understood that at this time ours was not the task of developing the principles of or determining the continuing need for a relative value index.

The task is well enough along to insure its presentation to you for the September meeting of the House of Delegates of the Utah State Medical Association. When our goal is achieved, it is to be hoped that future revisions will be relatively minor as far as time and scope are concerned.

A.M.A. Delegate report

Dr. Drew Petersen: As you will remember, a resolution was passed at the House of Delegates last September on the use of tobacco. This was

presented at the House meetings, the Clinical Session in Washington, D. C., last December and I talked to this resolution in the reference committee and as you will note in the report, there, of course, were several rebuttals. Most of them came from the "You-all Delegates" from down South and they had some good arguments, needless to say. A member of the Board of Trustees appeared and stated that the Council on Drugs had been authorized by the Board of Trustees to assemble and evaluate existing medical evidence with respect to the effects of smoking. So the resolution, of course, was not then adopted by the House but it was referred back to the Board of Trustees for their further consideration.

Now there were several other important points and one of the most important, in my opinion, was the report of the special committee appointed by the Board of Trustees of the A.M.A. on scholarships and loans to worthy, likely medical students. As you know, our problem has become increasingly difficult, attracting worthy applicants to medical school because of other engineering fields, electronics, what not. If any of you wish to get the fine details of this, the information is available. I have a copy of it. It was a real thick report and very, very comprehensive and well done so I am not going to go over that.

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Pyridoxine HCl (B ₆)	1 Int. Unit
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The problem of foreign medical school graduates was discussed again and, of course, then the big factor of the A.M.A. dues increase, which most of you realize—you can all read exactly what the situation is and why the Board of Trustees had recommended that we have an increase in dues and, of course, the old problem of the health care for the aged and, as you know, the A.M.A. still backs the Mills-Kerr type of legislation.

(The speaker then referred to his printed report.)

Published reports of the various committees were reviewed and amended. These reports, far too exhaustive to be published here, may be reviewed by members at the offices of the Utah State Medical Association.

Resolutions

The following resolutions were approved:

RESOLUTION NO. 1

WHEREAS, the Social Security system for the provision of retirement income and death benefits insurance should be debated by the medical profession as an unsuitable or suitable method for its members and clearly is not a state but a national matter for legislation, and

WHEREAS, rightly or wrongly, Social Security is the law of the land and applicable at present to nearly all Americans, and

WHEREAS, scattered surveys and polls have been taken within certain groups of our medical profession, variously worded and interpreted by the different county and state

societies, and

WHEREAS, the Delegates to the A.M.A. from our fifty states are either not instructed on how to vote by their societies on Social Security for doctors, represent only their own personal viewpoint, or are instructed from state polls which are qualified in some particular respect by the wording used in these polls; now therefore, be it

RESOLVED, that the Utah State Medical Association request the A.M.A. to conduct a nationwide poll of all physicians, A.M.A., and non-A.M.A. members, concerning each doctor's opinion about joining or not joining the Social Security program. This nationwide poll should be identically worded in all states and the results should be made available to all M.D.'s, and therefore, be it further

RESOLVED, that our Delegate introduce this Resolution into the House of Delegates to the A.M.A. asking for a nationwide poll and that the question shall be a plain question of fact: "Should doctors have Social Security or should doctors not have Social Security?"

RESOLUTION NO. 2

WHEREAS, it is the opinion of many county and state medical officers that procedures for hearing of and prosecution of grievances against doctors, as evidenced by written county medical society constitutions, are both cumbersome and unworkable in some instances, and

WHEREAS, in many small county medical societies it is unfair to ask fellow doctors, closely associated with a doctor who is charged with an offense, to sit in judgment upon the accused doctor, or if not unfair, these doctors may be accused themselves of benefiting by rendered adverse judgments; now, therefore, be it

RESOLVED, that the Constitution and By-Laws Committee be instructed to present to the House of Delegates in the next general session of the House of Delegates of the Utah State Medical Association, appropriate changes in the Constitution providing for a new code of discipline in accordance with the foregoing, and be it further

RESOLVED, that upon approval of such changes by the House of Delegates, all county medical societies of the Utah State Medical Association shall revise their constitution and by-laws accordingly.

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WYOMING

"Better Informed" public material available

Francis A. Barrett, M.D., President of the Wyoming State Medical Society, has announced completion of a program of public communication designed to acquaint the people of Wyoming with the latest advances and technics in the field of medicine.

Motion pictures and other illustrative materials have been made available to each county medical society and every doctor in Wyoming has been alerted to the part he should play in this informative and educational program. An early response is anticipated by civic organizations and clubs in communities throughout the state to assist in carrying out this approach toward a "better informed" public.

Sheridan student National winner

An 18-year-old senior from Sheridan High School has won second place in a national essay contest sponsored by the National Association of Physicians and Surgeons, according to Francis A.

Barrett, M.D., President of the Wyoming State Medical Society.

The winner, Carol Anne Hoaglan, will receive a cash award of \$500.00. Title of her essay is "The Advantages of Private Medical Care."

Miss Hoaglan serves as editor of the Sheridan High School student newspaper and is a member of the National Honor Society.



MEDICAL SCHOOL NOTES

Medicolegal Institute at Crested Butte

Crested Butte, Colorado, has been chosen by the Law-Science Academy of America as the location for conducting its unique Summer Instructional Program. Subjects include: Instruction in Legal Medicine, Personal Injury Problems and Medicolegal Trial Technic, with lecturers who have been chosen from among recognized authorities in the medical and scientific fields. Each of the nine weeks of this program will be a course in itself.

All physicians, lawyers, claims personnel and

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All physicians interested in the care of infants and children are invited to register.
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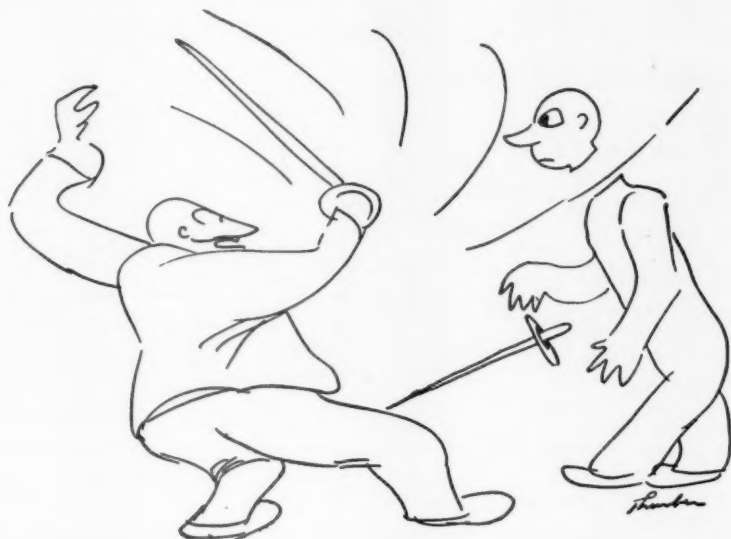
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others professionally concerned with personal injury problems are cordially invited to attend these sessions.

Write for full information concerning registration fees, living accommodations and details of courses offered to Dr. Hubert Winston Smith, Director, The Law-Science Institute, Townes Hall, University of Texas Law School, 2500 Red River, Austin 5, Texas.



American Board of Obstetrics and Gynecology

Applications for certification in the American Board of Obstetrics and Gynecology, new and re-opened, Part I, and requests for re-examination in Part II are now being accepted. All candidates are urged to make such application at the earliest possible date. Deadline date for receipt of applications is August 1, 1961. No applications can be accepted after that date.

Candidates are requested to write to the office



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of the Secretary for a current bulletin if they have not done so, in order that they might be well informed as to the present requirements. Application fee (\$35.00), photographs, and lists of hospital admissions must accompany all applications.

After July 1, 1962, this Board will require a minimum of three years of approved progressive residency training to fulfill the requirements for admission to examination. After the above date, training by preceptorship will no longer be acceptable.

Diplomates of this Board are urged to notify the office of the Secretary, Robert L. Faulkner, M.D., 2105 Adelbert Road, Cleveland 6, Ohio, as soon as possible of changes in address.



Blue Shield

Enrollment in the nationwide Blue Shield Plans surpassed the 47,000,000 member mark at the end of 1960, the National Association of Blue Shield

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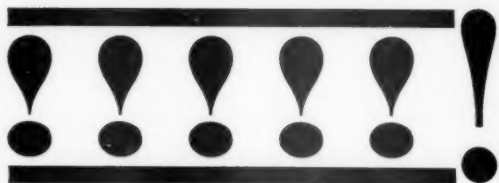
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The use of wine, especially in moderation, is as old as written history. Social scientists claim that no usage of any kind persists unless it serves an important function.

Stress Relief Studies—Recent research by Greenberg, Carpenter and Associates at Yale University's Laboratory of Applied Physiology, helps explain one reason for the popularity of wine in nearly all cultures and all nations for thousands and thousands of years.

It was found that as little as 3 ounces of a California Burgundy could lower the emotional tension index in normal humans exposed to controlled conditions of extreme stress.

The tranquilizing effect of wine appears to be greater and yet smoother than that produced by most other beverages, and perhaps safer than that of the usual synthetic pill.

Other Physiological Actions and Clinical Roles—The above is just one of the many interesting research studies now being conducted on the physiological effects of wine.

Based on recent findings, the modern Rx uses for wine—in convalescence, cardiology, urology, geriatrics—are discussed in “Uses of Wine in Medical Practice.” Wine Advisory Board, 717 Market Street, San Francisco 3, California.

*Silverman, M.: 48th Quarterly Meeting, Soc. Medical Friends of Wine, Jan. 13, 1960



Plans reported in Chicago last month. Total membership in the 74 medical-surgical Plans reached 47,084,988 on December 31, 1960, representing an enrollment of one out of every four Americans, and nearly 15 per cent of the total Canadian population.

Blue Shield—announcement

The National Association of Blue Shield Plans has gone on record as supporting the American Medical Association in its endorsement of the Kerr-Mills Medical Aid for the Aged Law passed by Congress in 1960. This action by representatives of the nationwide Blue Shield Plans was taken at their 1961 annual business meeting held April 16-18, at the Edgewater Beach Hotel, Chicago.

This resolution pertaining to the Kerr-Mills Bill was submitted by the Colorado Blue Shield Plan and called on Blue Shield Plans to make their administrative facilities available, through sponsoring medical societies, to state legislators in order to assist in the implementation of the new law at the state level.

I thought Ole Doc was a little off
When he gave me salts to cure my cough.
But Doc was right—he wasn't off
For now, By Gosh!—I'm afraid to cough.

John D. Davies, M.D. (Alamosa, Colorado)

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Malignant mesothelioma

Catherine W. Anthony, M.D., Moderator, Norman L. Welch, M.D., Resident in Pathology*

Although, until recently, certain authors have expressed a belief that there are no primary tumors of the mesothelium, evidence has now accumulated to refute this stand. It has been demonstrated that the removal of solitary tumors in mesothelial structures results in permanent cure in some cases and this certainly could not have occurred if these neoplasms had been metastatic. Also, the histologic pattern of primary mesotheliomas is considered to be distinctive¹. Today we wish to present two previously unrecorded cases of primary mesothelioma, one of the pleura and one of the peritoneum.

Case 1: This white female, D. B., was 55 years of age when she was first seen in 1954, because of recurrent vague abdominal pain of one year's duration. Past history was noncontributory. Physical examination was normal and routine blood and urine studies were within normal limits. The patient was operated upon and an apparent low grade inflammatory process was found in the peritoneum of the pelvis. A small nodule found in the omentum was removed and a bilateral salpingo-oophorectomy and pan-hysterectomy was performed. Microscopic examination revealed no tumors of the pelvic organs; however, the mass in the omentum proved to be papillary form of a malignant mesothelioma. The thin papillary stalks were covered with cuboidal epithelial cells which were quite uniform, eosinophilic and showed distinct hyperchromatic nuclei with very prominent nucleoli (Fig. 1). There was invasion of the underlying connective tissue. The patient did well for two years following the operation and then began to have recurrent abdominal pain. In 1958, the patient again underwent surgery and was found to have widespread tumor implants in the peri-

toneum. Radioactive gold was placed into the abdominal cavity. The patient gradually developed ascites, shortness of breath, weight loss, ankle edema and bilateral pleural effusions. The pleural fluid was noted to reform rapidly after it was removed. She expired on March 6, 1960, and an autopsy was performed which revealed almost complete replacement of all peritoneal and pleural surfaces by a nodular neoplasm. There was marked pleural effusion, with resulting severe atelectases of both lungs, and ascites. No other primary tumors were found and the tumor presented the same histologic pattern as was found at the time of the original surgery. Stains for mucin were negative but there were PAS positive granules present in the cytoplasm of many of the tumor cells.

Case 2: E. R., a 39-year-old white male, was

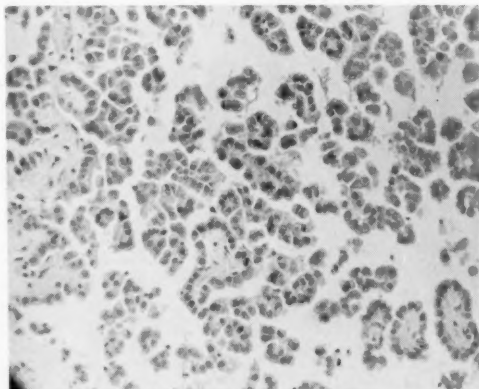


Fig. 1. Papillary mesothelioma of the peritoneum showing hyperchromatic nuclei and distinct nucleoli. (H. and E. x 430.)

*Supported by grant from the Frieda L. Maytag Memorial Cancer Fund, Colorado Division, American Cancer Society.

first seen on October 3, 1960, when he complained of pain in the right lateral chest of three weeks' duration. He had had shortness of breath during the two weeks preceding admission. There was no other significant history. Physical examination was normal except for decrease in resonance and breath sounds at the right lung base. Laboratory studies were all within normal limits except for the erythrocyte sedimentation rate which was 21 mm. per hour. X-ray examination of the chest showed a pleural effusion in the right pleural space. Bronchograms were normal. The pleural fluid was removed three times and each time cytologic studies were done but were negative for malignant cells. A pleural needle biopsy was inconclusive. On October 18, a thoracotomy was performed and a diffuse nodular tumor involving both the visceral and parietal pleura was found. The pleura was stripped and microscopic examination of the tumor showed it to be a malignant mesothelioma composed primarily of epithelial elements but also containing small areas with fibrous structure (Fig. 2). Studies for primary tumors elsewhere in the body were negative.

Dr. Catherine W. Anthony: Cytology of pleural fluid is sometimes difficult to evaluate because

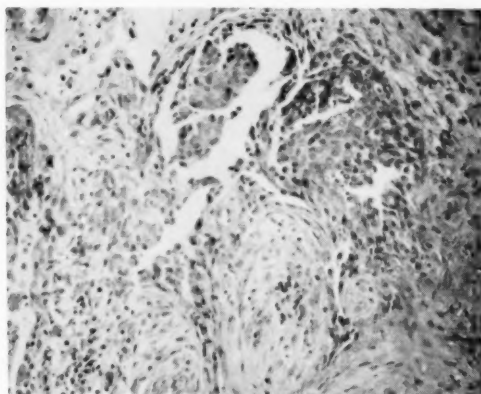


Fig. 2. Pleural mesothelioma demonstrating both fibrous and epithelial elements. (H. and E. x 430.)

irritation of the pleura will cause shedding of atypical cells. As a rule, therefore, a positive diagnosis of malignancy is given only if groups of neoplastic cells are seen. This necessitates not only the presence of tumor on the pleura but of exfoliation of these cells. Occasionally, repeated aspiration will yield a positive diagnosis in one aspirate after several previous ones have been negative. The positive result may come about because of the release of groups of cells secondary to the trauma associated with repeated withdrawing of the fluid.

An interesting recent development is that lactic dehydrogenase is present in a much higher level in fluid from a cavity where a malignancy is present than the level found in the plasma. In a benign process the levels in the cavity fluid and plasma are the same.

Dr. H. B. Kennison, Jr.: This case presented us with the problem of idiopathic pleural effusion, that is, until the diagnosis was made. The differential diagnosis of pleural effusion includes three general mechanisms—these are inflammatory processes, mechanical disorders, and neoplastic disease involving the pleura. Most pleural effusions due to inflammation involve a direct invasion of the pleura by pathogenic organisms. Certain generalized inflammatory disease processes, however, can produce a pleural effusion. These include disseminated lupus erythematosus, uremia, rheumatoid arthritis, rheumatic fever and, in fact, any inflammatory process involving the lung. In considering the inflammatory type, there are three major types of pleural reaction. The first of these is the development of fibrous adhesions which produce painful pleurisy. The second is the production of a fibrinous exudate or effusion which has a specific gravity greater than 1.018 and a protein content of over 4 per cent. The third type of pleural reaction is the production of purulent exudate. Examination of pleural fluid in the two types of inflammatory reaction where there is exudate quite often reveals the diagnosis. If no organisms can be cultured from the pleural fluid immediately one should suspect tuberculosis as the cause of the effusion. Also, one must consider

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generalized inflammatory diseases as mentioned. It is important to study the total problem before going so far as to do a thoracotomy. In the case under discussion, study of the fluid and many other diagnostic procedures including bronchoscopy and pleural biopsy revealed no diagnosis so thoracotomy was advised.

Pleural effusion produced by mechanical disturbance is very commonly due to organic heart disease. In this instance, the fluid accumulation is referred to as a hydro-thorax. The fluid has specific gravity of less than 1.014. Examination reveals evidence of increased venous pressure. Quite often an electrocardiographic abnormality or auscultatory and radiographic findings make the diagnosis of organic heart disease quite evident. Hemorrhagic effusion is due to malignant tumor involving the pleura in 85 per cent of the cases. Also, pulmonary infarction may produce hemorrhagic effusion. Other miscellaneous causes of pleural effusion include trauma, generalized hemorrhagic disorders and chylothorax. Chylothorax is evident upon examination of the fluid and is usually due to malignant involvement of the thoracic duct but may follow trauma to the chest. A chyloid effusion is a descriptive term referring to a milky colored fluid and is not necessarily indicative of a true chylothorax.

Dr. Norman L. Welch: Primary mesotheliomas have been reported as originating in the peritoneum, the pleura and the pericardium. The histologic pattern may be fibrous, epithelial, or mixed², and it has been well demonstrated by tissue culture technics that the fibrous and epithelial types are derived from the same cells, namely, mesothelial cells³. It is easy to identify some tumors as malignant; however, at times benign appearing tumors will recur, metastasize, and cause death. Therefore, a benign diagnosis is made with reservation. Mesotheliomas generally metastasize widely by lymphatic routes, but a few blood-borne metastases may occur. The treatment of mesotheliomas involves complete surgical excision of localized tumors and palliative treatment of the diffuse type. There is no distinctive clinical picture; however, patients with pleural mesotheliomas may have a nonproductive dry cough, dyspnea, pain and rapidly accumulating pleural fluid which is mucoid and composed largely of hyaluronic acid. Although it was not demonstrated in either of the cases presented today, some patients will present with symptoms of hypoglycemia identical to those of an islet cell tumor of the pancreas. The question of the mechanisms of the hypoglycemia is unresolved but the two theories are first, that the tumor produces an insulin-like substance³ and, second, that the tumor metabolizes carbohydrates so rapidly that hypoglycemia occurs⁴.

Dr. Kenneth D. A. Allen: There is a radio isotope test available which is useful in differentiating pleural effusions produced by benign lesions



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from those produced by malignant neoplasms. X-ray therapy in the treatment of mesotheliomas is only palliative and aimed primarily at reducing the amount of fluid produced by the tumor. In the second case presented today, we elected not to treat this patient with x-ray because it would involve treatment of the entire chest since there was no localization and, of course, this is not ideal for x-ray therapy. There was no opportunity to put gold into the chest cavity as the pleura had been stripped and there was no cavity remaining.

Dr. David E. Dines: Dr. Allen, wouldn't it be helpful if clips had been placed in the areas of the tumor at the time of surgery so that x-ray therapy could be localized?

Dr. Allen: This is a good thought and might be helpful in future cases. However, in today's case the tumor was too widespread to make this practical.

Dr. Kennison: In the second case today we have started treatment with nitrogen mustard and if any localized areas of tumor recur we will treat these with x-ray.

Dr. Kenneth C. Sawyer: Isn't it true that some of these patients with mesotheliomas will have arthralgia similar to rheumatoid arthritis?

Dr. Raymond W. Hammer: These patients may have pulmonary osteo-arthritis and some of them have rheumatoid distribution of pain and tenderness. Following the removal of the mesothelioma there may be dramatic loss of all symptoms of arthritis.

In summary, two cases of malignant mesothelioma have been presented; one originated in the pleura and the other in the peritoneum. The clinical manifestations, pathology, differential diagnosis and treatment have been discussed.

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